

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10x GENOMICS, INC.,

Petitioner,

vs.

BRUKER SPATIAL BIOLOGY, INC.,

Patent Owner.

Case: IPR2023-01298

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

VIDEOTAPED DEPOSITION OF DAVID SHERMAN, Ph.D.

3223 South State Street, Ann Arbor, Michigan

Wednesday, October 30, 2024

8:54 a.m.

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Pages: 1 - 79

Stenographically Reported By:

Alison C. Webster, CSR-6266, RPR, RMR, CRR, RDR

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DEPOSITION OF DAVID SHERMAN, Ph.D.

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DAVID SHERMAN, Ph.D.,

was thereupon called as a witness herein, and after
having first been duly sworn to testify to the truth,
the whole truth and nothing but the truth, was
examined and testified as follows:

MR. HOLMAN: Good morning, Dr. Sherman.

THE WITNESS: Good morning.

MR. HOLMAN: My name is David Holman. I'm
with the law firm Sterne Kessler Goldstein & Fox. I
represent petitioner 10x Genomics. And with me here
today is my colleague, Pratibha Khanduri, also from
Sterne Kessler.

EXAMINATION

BY MR. HOLMAN:

Q. Would you please state your full name for the record?

A. David Howard Sherman.

Q. And what's your place of residence, Dr. Sherman?

A. Ann Arbor, Michigan.

Q. Have you ever been deposed before?

A. Yes.

Q. How many times?

A. Probably 20 or so.

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1 Q. What was the last -- when was the last time you were
2 deposited?

3 A. Sometime during the pandemic. It was virtual.

4 Q. So maybe about four years ago? 2020 time frame?

5 A. 2021 -- 2021 probably, yeah.

6 Q. Do you recall the subject matter of that case that you
7 were deposited in?

8 A. It was an arbitration.

9 Q. Was it a patent matter?

10 A. Yes.

11 Q. And what technology did that concern?

12 A. Various -- in that case, monoclonal antibodies.

13 Q. How about trial testimony, have you ever testified at
14 trial as an expert witness?

15 A. Yes.

16 Q. How many times have you testified at trial?

17 A. Probably six or seven.

18 Q. When was the last time you testified at trial?

19 A. 2019.

20 Q. All right. And what was the subject matter of that
21 trial?

22 A. It involved the genetics of organisms that produced
23 botulinum toxin.

24 Q. And did that -- was that a patent dispute as well?

25 A. That was a trade secret matter.

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1 Q. All right. So you've done this a few times.

2 You've been sworn in today. You understand

3 that you're here testifying under oath and under

4 penalty of perjury in the United States?

5 A. Yes.

6 Q. And you understand that means you're here to testify

7 truthfully and accurately regarding the questions I

8 ask you today?

9 A. Yes.

10 Q. Is there any reason you cannot testify truthfully and

11 accurately today?

12 A. No.

13 Q. We have a court reporter here with us transcribing our

14 conversation. Do you understand that the transcript

15 from today's deposition will be entered into the

16 record and will become public?

17 A. Yes.

18 Q. As our court reporter is transcribing our conversation

19 today it's going to be important that we not speak

20 over each other or interrupt each other, so I'm going

21 to do my best to wait until you finish your answer

22 before I respond, and I ask that you do the same, let

23 me finish my question before you begin your answer.

24 A. Understood.

25 Q. I ask that if you don't understand a question, that

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1 you ask me for clarification or explanation rather
2 than asking your counsel. Do you understand that?

3 A. I do.

4 Q. Do you agree to do that?

5 A. Yes, I do.

6 Q. During this deposition, you understand you're not
7 permitted to speak to anyone about the substance of
8 your testimony today until this deposition is
9 concluded?

10 A. Yes, I do.

11 Q. And do you agree to do that?

12 A. Yes.

13 Q. We'll take breaks during reasonable intervals today.
14 So if you need a break, just ask me for a break, we'll
15 be happy to take one. All I ask is that if there's a
16 question pending, that you answer the question before
17 we take a break.

18 A. Okay.

19 Q. Do you understand that?

20 A. I do.

21 Q. During this deposition your counsel may object to some
22 questions. If counsel objects to a question, do you
23 understand that you still must answer my question
24 unless your counsel specifically instructs you not to

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answer?

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1 A. Understood.

2 Q. Okay. Dr. Sherman, do you understand why you're being
3 deposited today?

4 A. Yes.

5 Q. What is your understanding of the reason for your
6 deposition today?

7 A. This is an IPR matter and there are various matters
8 that have been raised between 10x Genomics and
9 following the submission to the board. The board
10 came back with various responses, and so I'm here to
11 answer questions from you about those questions.

12 Q. Do you understand what an IPR matter is?

13 A. Yes.

14 Q. What's your understanding of an IPR matter?

15 A. There's one -- there are two companies and two
16 patents and one company raises issues about the other
17 company's patents and disputes those patents, and
18 that occurs in the institution -- the review board, I
19 guess, the USPTO. And the company raising the
20 questions about the other patent, you write a report
21 and describe their concerns or issues and submit it
22 to the board, and the board then reviews that and
23 issues a reply.

24 Q. You said "there are two companies." Is one of the
25 www.LexitasLegal.com/Premier Lexitas companies you're referring to, is that 10x Genomics?

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1 A. One company is 10x Genomics.

2 Q. And what's your understanding of the other company?

3 A. NanoString.

4 Q. And you understand NanoString was recently acquired by

5 a company called Bruker Spatial -- let's just call it

6 Bruker for today. Do you understand that?

7 A. Yes, I do.

8 Q. So today I may refer to the patent owner as NanoString

9 or I may refer to the patent owner as Bruker.

10 A. Okay.

11 Q. Do you understand that?

12 A. I do. Yeah.

13 Q. You also mentioned there are -- you said there were

14 two companies and two patents. Do you understand

15 what -- what do you mean by the two patents you're

16 referring to there?

17 A. Well, the '689, and I believe it's called Chell.

18 Q. Okay. The Chell -- the Chell, are you referring to

19 the Chell patent application?

20 A. Application. Correct. That's right. Patent

21 application.

22 Q. When did patent owner first contact you to retain your

23 services for this IPR?

24 A. I believe it was sometime over the summer.

25 Q. Summer of 2024?

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1 A. Right.

2 Q. And who contacted you?

3 A. An attorney at Weil.

4 Q. Do you remember the name of the attorney?

5 A. I'm not sure exactly who made the initial contact.

6 I'd have to go back to my records.

7 Q. But you think it was an attorney from the law firm

8 Weil that contacted you?

9 A. Well, I was actually contacted by an expert witness

10 service about a matter, and it was this matter, and I

11 spoke to an attorney at Weil.

12 Q. What's the name of the expert witness service?

13 A. I think it's called IMS.

14 Q. Do you regularly consult through IMS with expert

15 witness services?

16 A. It's rare. Occasionally I'm contacted, yeah. So

17 this was one -- this was a situation where I was.

18 Q. Okay. Before you were contacted summer of 2024 about

19 this case, were you aware of a patent dispute between

20 10x Genomics and NanoString?

21 A. No.

22 Q. Before you were contacted in the summer of 2024 for

23 your services in this IPR, were you aware of any

24 litigation between 10x Genomics and NanoString?

25 A. No.

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1 Q. And aside from serving as an expert witness in this
2 IPR, do you have any other professional relationship
3 with NanoString?
4 A. No.
5 Q. Do you have any other professional relationships with
6 Bruker?
7 A. No.
8 Q. Do you have any research funding from NanoString?
9 A. No.
10 Q. Do you have any research funding from Bruker?
11 A. No.
12 Q. Do you own stock in either company?
13 A. No, I don't.
14 Q. During the -- your work as an expert witness in this
15 IPR on behalf of NanoString, have you communicated
16 with anyone at NanoString other than counsel?
17 A. No.
18 Q. Have you communicated with anyone at Bruker other than
19 counsel?
20 A. No.
21 Q. Dr. Sherman, are you being compensated for your
22 testimony here today?
23 A. I am.
24 Q. What is your current consulting rate for your
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testimony today?

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1 A. I believe it's \$700 an hour.

2 Q. Have you submitted any invoices for your work in this

3 IPR?

4 A. Yes.

5 Q. What would you say is the total amount you've invoiced

6 up to this point?

7 A. I let my accountant handle all that. I'm really not

8 sure what that number is. All I could do is venture

9 a guess, which I'm reluctant to do.

10 Q. Can you give me a ballpark idea?

11 A. Probably between 15- and 20,000.

12 Q. All right. What did you do to prepare for today's

13 deposition?

14 A. So I read my declaration and the supporting documents

15 and, you know, went through that material. Reviewed

16 the 10x document raising issues that were submitted

17 to the board, reviewed some statements from the

18 board, board response, you know, so that -- that's a

19 general substance of what I did to prep.

20 Q. When you say that -- "the 10x document raising issues

21 that was submitted to the board," are you referring to

22 the petition for IPR?

23 A. I think that's what it's called.

24 Q. Okay.

25 A. Right.

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1 Q. You said you read your declaration and supporting
2 documents. Can you clarify a little bit about the
3 supporting documents? Which supporting documents did
4 you review?

5 A. There's some documents in the '689 which I also
6 reviewed. There are documents that are incorporated
7 by reference that I reviewed. So '456, I reviewed.

8 Q. When you were preparing for today's deposition, did
9 you review any documents that are not cited or listed
10 in your declaration?

11 A. No.

12 Q. All right. And just for the record, it doesn't look
13 like you have any materials or documents that you
14 brought with you to the deposition --

15 A. No.

16 Q. -- is that correct? Okay.

17 I'm going to hand you a copy of your
18 declaration. It's been marked as Exhibit 2006.

19 A. Thank you.

20 ENTERED INTO THE RECORD:
21 PREVIOUSLY MARKED EXHIBIT 2006
22 9:08 a.m.

23 BY MR. HOLMAN:

24 Q. All right, Dr. Sherman, do you recognize this
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document?

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1 A. I do.

2 Q. And do you recognize this document as your declaration
3 that you submitted in this IPR?

4 A. Yes.

5 Q. Could you please turn to page 74, the last page of the
6 document?

7 Could you please confirm that this is your
8 signature?

9 A. Yes, it is.

10 Q. And you signed this declaration on August 26th, 2024;
11 is that correct?

12 A. Right.

13 Q. All right. When you were preparing this declaration
14 did you read all of the exhibits that were cited in
15 this declaration?

16 A. Yes, I did.

17 Q. In preparing this declaration, did you rely on any
18 documents that are not cited in this declaration?

19 A. No.

20 Q. Would you say if a document were important for your
21 opinions in this declaration you would have cited it
22 in this declaration?

23 A. Yes, I would have.

24 Q. Approximately how many hours did you spend preparing
25 this declaration?

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1 A. I'd have to -- I'd have to look back at my records.

2 Q. Can you take a guess?

3 A. 15 to 20 hours.

4 Q. Did you meet with anyone in preparing your

5 declaration?

6 A. Yes.

7 Q. With whom did you meet?

8 A. I met with three lawyers from -- well, primarily two

9 lawyers from Weil, and Derek would join as well.

10 Q. Who are the other two lawyers from Weil?

11 A. Concord, I believe his last name is Chen, and then

12 Karnik. I'm afraid I don't recall his last name.

13 Q. And how many times did you meet with the lawyers from

14 Weil in preparing your declaration?

15 A. We'd meet every couple of weeks or so.

16 Q. About how many meetings was that?

17 A. Four to six, perhaps.

18 Q. And when you were preparing your declaration, did you

19 meet with anyone who was not a lawyer?

20 A. No.

21 Q. Okay. Dr. Sherman, you have a bachelor of arts in

22 chemistry; is that correct?

23 A. That's right. Yes.

24 Q. And you have a Ph.D. in organic chemistry; is that

25 right?

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1 A. That's correct.

2 Q. Okay. Where are you currently employed?

3 A. University of Michigan.

4 Q. And what's your title there at University of Michigan?

5 A. I am the Hans Vahlteich professor of medicinal

6 chemistry. I am a professor of microbiology and

7 immunology. I am a professor of chemistry. And I am

8 a research professor at the Life Sciences Institute

9 where my laboratory is located.

10 Q. So you have a research laboratory there at University

11 of Michigan?

12 A. Right.

13 Q. What's the -- how would you describe the nature of

14 your research?

15 A. Broadly, I'm interested and study drug discovery,

16 molecules to develop pharmaceuticals.

17 Q. And does that research involve synthetic chemistry?

18 A. It does. It involves synthetic chemistry and other

19 molecular biology, molecular genetics. Lots of --

20 it's a very multidisciplinary topic.

21 Q. Would you characterize part of your research as

22 focusing on drug discovery?

23 A. Part of it is, yes.

24 Q. What would another part of your research be

25 characterized as?

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1 A. So drug discovery includes a variety of topics. Not
2 only finding the molecules that are bioactive, but
3 understanding exactly what their target is, what they
4 bind to. So there's a whole component of targeting
5 identification; where does the molecule go in the
6 cell or the tissue to bind it and do its work. And
7 that involves all sorts of methods, including the
8 ones that are relevant to this matter.

9 I study how the molecules are made, if they
10 come from microorganisms, so in addition to synthetic
11 chemistry we use bacteria and fungi to produce our
12 molecules, and that's a whole other topic in terms of
13 engineering the systems to make the molecules we want.

14 And so we study that also in detail.

15 Q. Do you have a relationship with a company called
16 Alluvium Biosciences?

17 A. I don't have a relationship with them, no.

18 Q. Have you ever had a relationship with a company called
19 Alluvium Biosciences?

20 A. No.

21 Q. Have you ever consulted for a company called Alluvium
22 Biosciences?

23 A. No.

24 Q. Do you have a relationship with a company called

25 www.LexitasLegal.com/Premier Lexitas
PharmaForensics Laboratories?

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1 A. YES.

2 Q. What is your relationship with PharmaForensics

3 Laboratories?

4 A. I am the cofounder of PharmaForensics Laboratories.

5 Q. What is -- what is PharmaForensics Laboratories?

6 A. It's a lab that analyzes intellectual property

7 matters at a technical level.

8 Q. What kind of lab? Is that like a -- what kind of

9 laboratory is PharmaForensics Laboratories?

10 A. It has diverse capabilities, among them synthetic

11 chemistry, molecular biology. We'll do drug

12 analysis, drug dissolution, analytical chemistry,

13 HPLC mass spectrometry, ELISA assays, microbiology.

14 So depends, but it has broad capabilities.

15 Q. And when you said "it's a lab that analyzes

16 intellectual property matters at a technical level,"

17 what do you mean by analyzing intellectual property

18 matters?

19 A. So it will be or -- the managing director who's my

20 cofounder who runs the company, Jeff Kittendorf,

21 he'll be contacted typically by a law firm or a

22 company that's interested in analyzing, say, a drug

23 formulation or, let's say, a generic pharmaceutical

24 that there are questions about or a biosimilar that

25 www.LexitasLegal.com/Premier Lexitas there are questions about. He'll obtain the material

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1 and analyze it and whatever questions are being

2 raised, he'll attempt to answer those questions.

3 Q. Would you say -- is it fair to characterize the work
4 performed at PharmaForensics Laboratories as focused
5 on supporting litigation efforts?

6 A. Sometimes. Sometimes. Sometimes they're contacted
7 by pharmacists who have gotten, let's say, calls from
8 patients with concerns about their generic
9 pharmaceuticals, and so the company will actually
10 analyze the actual drug composition to assess whether
11 it's what it's supposed to be.

12 Q. What portion of the laboratory testing at
13 PharmaForensics Labs would you say goes toward
14 litigation support?

15 A. It really depends from year to year. It varies
16 considerably.

17 Q. Do you receive income from PharmaForensics
18 Laboratories?

19 A. I do. I -- yes, I do.

20 Q. How much of your personal income -- what proportion of
21 your personal income is generated or provided by
22 PharmaForensics Laboratories?

23 A. Probably about 5 percent.

24 Q. In your work, your research, drug discovery, drug
25 targets, biosynthesis pathways I think you said --

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1 A. Right.

2 Q. -- do you -- have you used spatial transcriptomics

3 methods in that research?

4 A. We've -- yes. In fact, some of my earliest work in

5 this area was directed towards understanding the

6 spatial location of particular regulators that

7 control the production of drug molecules in bacteria.

8 Q. And was that at the transcript level or the protein

9 level?

10 A. It was at the protein level.

11 Q. What methods did you use for that -- for that

12 research?

13 A. At that time it was essentially engineering a GFP

14 gene and then using confocal microscopy to identify

15 the location of that fluorescent signal in the cell.

16 Q. Would you -- is it fair to characterize that work as

17 proteomics?

18 A. I wouldn't characterize that as proteomics because we

19 weren't studying the protein. We were interested in

20 the spatial location of that protein.

21 Q. Do you have any experience in your research using

22 commercial products for spatial transcriptomics?

23 A. Yes. For my HIV drug discovery project, yes.

24 Q. What products -- product or products did you use in

25 that research?

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1 A. We -- at Michigan, we have core laboratories that
2 have both 10x Genomics and NanoString's capabilities,
3 so I have used them both.

4 Q. Let's start with the 10x products, which products are
5 you referring to?

6 A. Visium.

7 Q. Do you know specifically which Visium product?

8 A. No.

9 Q. Do you know if it was a Visium fresh version -- fresh
10 frozen or Visium FFPE?

11 A. It was -- I mean, based on what we were doing, it
12 would have been the fresh frozen.

13 Q. All right. And then how about the NanoString
14 products? What NanoString products have you used
15 there?

16 A. I believe it's called the GOMX? Is that the name of
17 it? Yeah.

18 Q. And what research did you use the GOMX products in?

19 A. Same.

20 Q. Same?

21 A. Yeah.

22 Q. HIV?

23 A. Sort of comparing the two.

24 Q. When did you perform -- when did you carry out this
25 research?

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1 A. In the last 9 to 12 months.

2 Q. Have you published this research?

3 A. Not yet. We're just working on the manuscript.

4 Q. You said you did this research in the last 9 to 12

5 months; is that right?

6 A. That's right.

7 Q. Can you be more specific when you used these products?

8 A. It probably started last November, December.

9 Q. And were you using -- you mentioned you were comparing

10 these two products; is that right?

11 A. Right.

12 Q. So were you using both Visium and the GOMX product

13 concurrently last November and December?

14 A. That's my memory, but I would have to go back to my

15 records to pinpoint.

16 Q. All right. When you were preparing your opinions in

17 your declaration, did you review the Patent Trial and

18 Appeal Board's decision on institution in this IPR?

19 A. You mean their response to the petition? Is that

20 what you mean?

21 Q. Yes. Let's take a look at your declaration. I think

22 that will be helpful.

23 A. Sure.

24 Q. So if you can -- in your declaration, if you could

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turn to page 5, paragraph 14.

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1 A. I'm there.

2 Q. All right. And then you state there, "In forming my

3 opinions, I have reviewed the following documents and

4 materials," and you provide a bulleted list of

5 documents there. I'm asking you about the

6 second-to-last bullet point, the board's institution

7 decision in this matter, Paper 14.

8 A. Right.

9 Q. So just to make sure we're clear here, so when you

10 were preparing the opinions in your declaration, did

11 you review this board institution decision Paper 14?

12 A. Yes.

13 Q. And in reviewing that, did you review the board's

14 claim construction of the terms "nucleic acid probe"

15 and "collecting nucleic acid probes"?

16 A. I did review it.

17 Q. Did you agree with the board's construction of those

18 two terms?

19 A. Let's see...

20 Q. I'll help you out. You can go to paragraph 27 of your

21 declaration.

22 A. Right.

23 Q. Right. That last sentence of 27, "To the extent that

24 the Board's construction refers to the use of an

25 www.LexitasLegal.com/Premier Lexitas extension reaction to encode spatial information, I

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1 agree with the Board's construction."

2 What part of the board's construction do
3 you believe refers to "the use of an extension
4 reaction to encode spatial information" -- strike
5 that?

6 Let me ask this, just to make sure we're
7 clear. What part of the board's construction of
8 "nucleic acid probe" do you believe refers to the use
9 of an extension reaction to encode spatial
10 information?

11 A. I would have to go to the board's document to look at
12 that.

13 Q. Well, in your testimony here in paragraph 27 --

14 A. Uh-huh.

15 Q. -- the sentence before the sentence that you read, you
16 state that "The Board construed the term 'nucleic acid
17 probe' to refer to an oligonucleotide comprising a
18 target binding domain that binds to one or more target
19 analytes, and is modified after collection to comprise
20 a location-identifying nucleic acid sequence for use
21 in identifying the location of the target analyte."

22 Did I read that correctly?

23 A. Yes.

24 Q. And is that your understanding of the board's

25 construction of "nucleic acid probe"?

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1 A. It is.

2 Q. Okay. So what part of that construction do you
3 believe refers to the use of an extension reaction to
4 encode special information?

5 A. So the -- there's a -- there's a probe that binds the
6 target, and then there's a location-identifying
7 nucleic acid, and an extension would essentially be
8 conducted to essentially create the nucleic acid that
9 covers them.

10 Q. Okay. And so is there a portion of the board's
11 construction here, as you've described it in your
12 testimony, that refers to use of an extension reaction
13 to encode special information?

14 Are you referring -- strike that.

15 Are you referring -- when you say, "To the
16 extent that the Board's construction refers to the use
17 of an extension reaction to encode spatial
18 information," are you referring to the board's
19 language where it says the nucleic acid probe is,
20 quote, modified after collection to comprise a
21 location and to define nucleic acid sequence, end
22 quote?

23 A. So you're looking above. Right?

24 Q. Correct.

25 A. So the board construed the term "nucleic acid probe"

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1 to refer to a nucleotide comprising a target binding
2 domain that binds to one or more target analytes and
3 is modified after collection to comprise a
4 location-identifying nucleic acid. Right.

5 Q. And when you are saying, right, the -- I just want to
6 make sure we're clear for the record, so I just want
7 to ask the question.

8 A. Well, I state that the board's construction refers to
9 an extension reaction.

10 Q. Well, you state, "To the extent that the Board's
11 construction refers to...an extension reaction," and
12 I'm asking you what part of the board's construction
13 is referring to extension reaction? Is that the
14 "modified after collection" language? And I think you
15 said that's correct. Is that...

16 A. "Modified after collection"?

17 Q. The board's construction, the sentence above your last
18 sentence in this paragraph, uses the language that the
19 nucleic acid probe "is modified after collection to
20 comprise a location-identifying nucleic acid
21 sequence."

22 A. Right. I see that.

23 Q. Do you see that language?

24 A. Right.

25 Q. Is it your opinion that that is what the board -- that

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1 is the construction that would refer to an extension
2 reaction to encode special information, as you've said
3 it in the next sentence?

4 A. So I'm not quite clear. You -- are you asking
5 whether that part connects to the next sentence? Is
6 that what you're asking?

7 Q. Yes. I'm asking whether that part connects to your
8 sentence stating that, to the extent the board's
9 construction refers to use of an extension reaction, I
10 agree with it.

11 A. Well, that sentence refers to what's above. To the
12 extent -- to the extent that the board's construction
13 refers to the use of an extension reaction to encode
14 spatial information, I agree with it. I mean, that's
15 what I say.

16 Q. In your opinion, does -- if a nucleic acid probe is
17 modified after collection to comprise a
18 location-identifying nucleic acid sequence, would an
19 extension reaction encoding spatial information meet
20 that criteria?

21 A. I mean, in that particular -- referring to that
22 particular example, it would. It doesn't exclude
23 other options.

24 Q. Do you believe you faithfully applied the board's
25 claim construction when rendering the opinions in your

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1

declaration?

2

A. As -- yes, as far as I understand.

3

Q. All right.

4

MR. HOLMAN: I'm going to hand you a

5

document that's been marked as Exhibit 1001. That is

6

the '689 patent.

7

ENTERED INTO THE RECORD:

8

PREVIOUSLY MARKED EXHIBIT 1001

9

9:36 a.m.

10 BY MR. HOLMAN:

11

Q. Do you recognize this document, Dr. Sherman?

12

A. I do.

13

Q. And you reviewed the '689 patent in forming the

14

opinions in your declaration. Correct?

15

A. That's correct.

16

Q. On the first page, the front page of this document,

17

there's -- on the right-hand column, there's an

18

abstract. Do you see that?

19

A. I do.

20

Q. And the abstract refers to a "user-defined region of a

21

tissue." Do you see that in the middle there?

22

A. "User-defined cell, and/or user-defined subcellular

23

structure within a cell." I think that's what you're

24

referring to.

25

Q. That's correct. What is your understanding of the

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1 689 patent's term "user-defined region"?

2 A. That the investigator has a set of objectives based
3 on what they're interested in studying, and it
4 includes defined reach of a tissue or a subcellular
5 structure of some sort.

6 Q. So is that -- would you characterize that as a
7 localized region within a larger sample?

8 A. That's one option.

9 Q. What's another option?

10 A. A location like a ribosome is one option; a tissue,
11 like a muscle or brain tissue, at a higher level, is
12 another option. It really depends on the question.

13 Q. Well, so I'm going to ask about the first example in
14 the abstract which says, "a user-defined region of a
15 tissue."

16 A. Uh-huh.

17 Q. So in that context, is a user-defined region of a
18 tissue a localized region within the broader tissue
19 sample?

20 A. Could be, yes.

21 Q. All right. Could you -- in the patent, the '689
22 patent, would you please turn to column 46?

23 A. Okay.

24 Q. All right. And so this is on the right-hand side.

25 www.LexitasLegal.com/Premier Lexitas
And if you could go down to line 51 of column 46 --

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1 A. Okay.

2 Q. -- and if you could just read lines 51 to 54 out loud

3 into the record, please.

4 A. Sure.

5 "As used herein, the terms 'region of

6 interest' and 'ROI'" -- and both of those in

7 quotations -- "are used in their broadest sense to

8 refer to a specific location within a sample that is

9 to be analyzed using the methods of the present

10 disclosure."

11 Q. Thank you.

12 So would you say -- is it your opinion that

13 a region of interest or an ROI is also a user-defined

14 region?

15 A. I would understand that to mean that the investigator

16 has defined that as a region of interest.

17 Q. Okay, I'm going to hand you another exhibit.

18 MR. HOLMAN: This document is marked as

19 Exhibit 1005. This is the So '456 reference.

20 ENTERED INTO THE RECORD:

21 PREVIOUSLY MARKED EXHIBIT 1005

22 9:43 a.m.

23 BY MR. HOLMAN:

24 Q. Do you recognize this document, Dr. Sherman?

25 A. Yes, I do.

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1 Q. And this is the So -- do you recognize this as the
2 So '456 document that you reviewed in preparing the
3 opinions in your declaration?
4 A. I do. Yes.
5 Q. All right. If you could please turn to Figure 9 in
6 this document. Let me know when you're there.
7 A. I'm there.
8 Q. All right. And you provided opinions on this figure
9 in your declaration. Right?
10 A. Correct.
11 Q. Figure 9 depicts a sequence of steps. Would you agree
12 with that?
13 A. I see that, yes.
14 Q. And the sequence of steps begins at the top of the
15 figure with a step 800. Do you see that?
16 A. Yes.
17 Q. And then proceeds downward, the next step being
18 step 810; is that right?
19 A. That's right.
20 Q. And then if you keep going down, there's another
21 step 815. Correct?
22 A. Correct.
23 Q. And then the next step is 820. Correct?
24 A. That's right.
25 Q. And then the last step, labeled step in this exhibit,

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1 is 825; is that correct? Or, sorry, the last step in

2 this figure is labeled as 825; is that correct?

3 A. That's right.

4 Q. All right. So I want to start at the top step at 810.

5 A. Okay.

6 Q. In step 810, So '456 depicts a molecule across the top

7 that's labeled as 910. Do you see that?

8 A. I do.

9 Q. And is molecule 910, is that the target DNA molecule

10 for this embodiment?

11 A. That's my understanding.

12 Q. All right. And just underneath that target DNA

13 molecule 910 there on the left-hand side, there's a

14 smaller molecule labeled as 920. Do you see that?

15 A. Right.

16 Q. And on the right-hand side there's another smaller

17 molecule labeled as 925. Do you see that?

18 A. Right.

19 Q. And molecule 920 and 925 are nucleic acid probes that

20 bind to this target DNA molecule 910; is that correct?

21 A. Could you repeat what you just said?

22 Q. Sure. Molecule 920 and 925 are nucleic acid probes

23 that bind to the target DNA molecule 910; is that

24 correct?

25 A. It looks like 930 and 940 bind to the target 910.

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1 Q. Okay. So the 930 -- so 930 is a portion of molecule
2 920; is that correct?

3 A. Right.

4 Q. And so the portion of 920 that binds to the target DNA
5 molecule is segment 930. Is that what you're saying?

6 A. That's what I'm saying, yes.

7 Q. And likewise on the right-hand side, the portion of
8 925 that binds to target DNA molecule 910 is segment
9 940; is that right?

10 A. That's correct.

11 Q. All right. So then the next step is step 815. Now,
12 in this step So '456 discloses that an
13 extension/ligation reaction is performed in situ using
14 these flanking probes 920 and 925.
15 Do you agree with that?

16 A. No.

17 Q. Okay. Let's take a look at -- keep your finger on
18 Figure 9 because we're going to come back to it --

19 A. Sure.

20 Q. -- but let's take a look at the disclosure from So.
21 And if you could turn to paragraph 182 in So '456.

22 A. 182?

23 Q. 182.

24 A. Sure.

25 Q. All right. And we were talking about step 815 in

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1 Figure 9. And so, midway down in paragraph 182

2 there's a sentence that begins, "At step 815, an
3 extension/ligation reaction is performed."

4 Do you see that sentence there?

5 A. I see the sentence.

6 Q. Okay. And I'm just going to read that sentence out
7 loud. So '456 discloses, quote, "At step 815, an
8 extension/ligation reaction is performed in situ
9 between the flanking capture oligonucleotides 920 and
10 925 across the region of interest."

11 Did I read that correctly?

12 A. You read it correctly.

13 Q. So now going -- looking back at Figure 9, when So
14 refers to extension/ligation reaction, what is being
15 extended, in your opinion?

16 A. That target sequence that includes the snip, the
17 mutation of interest.

18 Q. And is that extended from segment 930 or from segment
19 940?

20 A. It depends which -- what the direction of the gene
21 is. It will -- the preliminaries will go in 5 prime
22 to 3 prime direction, but there's no -- I don't see
23 any 5 prime or 3 prime here, so we have to surmise
24 one way or the other based on what end is what.

25 Q. So you're saying it's one of the two. It's either

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1 extended from the probe on the left towards the probe
2 on the right or it's extended from the probe on the
3 right towards the probe on the left.

4 A. It will be one or the other in a single direction
5 based where the 5 prime ended, where the 3 prime
6 ended, which they don't reveal here.

7 Now, I can surmise from the last figure
8 what it is -- from the bottom, what it is. But it
9 doesn't specifically state it, but it can be surmised
10 based on the 825 part of the figure.

11 Q. What enzyme -- strike that.

12 I think you said -- what enzyme performs
13 the extension? Is that the DNA polymerase?

14 A. DNA polymerase.

15 Q. Is that -- more specifically, would that be a
16 DNA-dependent DNA polymerase?

17 A. It would depend on the template, yes.

18 Q. If the template were target DNA, in that situation
19 would the polymerase enzyme used for extension be a
20 DNA-dependent DNA polymerase?

21 A. If it depends on DNA of that top fragment with the
22 snip, yes.

23 Q. So after one of these -- one of the two probes is
24 extended towards the other, the extended probe is then

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ligated to the other probe; is that correct?

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1 A. NO.

2 Q. What happens next after this extension occurs? What
3 is your understanding of what happens next?

4 A. I interpret this based on what's in the patent, is
5 that it's an extension reaction. There's no
6 ligation. Ligation has a very specific meaning and
7 that meaning -- they use the word "ligation," but
8 it's not a ligation because there's no ligase.

9 DNA polymerase doesn't perform a ligation
10 reaction. So they've used that term. They've used
11 it incorrectly. You can look at the patent, search
12 for the word "ligase," appears twice, and neither
13 time does it apply to this in terms of performing a
14 reaction that a ligase would perform.

15 Q. Would you agree that a POSA, before February 12th,
16 2018, would have a strong understanding and/or
17 experience ligating nucleic acids, including using
18 ligases? Correct?

19 A. A POSA would know what that is, but they would also
20 know that what they're saying is an extension
21 ligation is not a ligation in this matter because
22 there's no ligase. It's a DNA polymerase. That's
23 it.

24 Q. So in your view, if a document doesn't explicitly
25 depict a DNA ligase there must not be a DNA ligase in

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1 that disclosure, is that correct?

2 A. As I said, in the whole -- this whole document,
3 ligase is described twice. One of them is a
4 CircLigase, that's circular linear DNA circle, and
5 that ligase, which all ligases do, they conduct --
6 they make a covalent bond. That's the key of a
7 ligase is to make a covalent bond. That's what a
8 ligase does and that's a ligase reaction. That's not
9 described here. There's no covalent bond generated
10 because there's no ligase.

11 Q. You agree a person of ordinary skill in the art
12 generally understood how to use ligases and the
13 mechanism of action of ligases including T4 ligase,
14 for example.

15 A. I agree with -- that they would know what that is,
16 but they would also readily know that it wasn't
17 applied here because there's no ligase. There's a
18 polymerase.

19 Q. So let's go back to to paragraph 182 in the So '456
20 disclosure, if you still have your finger on that
21 page.

22 A. Page 37, 182?

23 Q. Yes, sir. And after the sentence that we were looking
24 at, the sentence that begins with "At step 815," the

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next sentence in this paragraph states, quote, "A DNA

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1 molecule 950 that is formed in the extension/ligation

2 reaction comprises universal capture region 935 and

3 SBS primer region 945."

4 Do you see that?

5 A. I do.

6 Q. And your opinion is that this DNA molecule that was

7 formed after the extension/ligation reaction was not

8 formed by a ligation; is that right?

9 A. It's not formed by a ligation. It's formed by an

10 extension.

11 Q. All right. But you just testified earlier that

12 there's an extension reaction taking place in this

13 figure. Correct?

14 A. There is. Yes.

15 Q. And what -- why is your -- what is the basis of your

16 understanding that there's a extension reaction taking

17 place?

18 A. They state that, and they want to generate through

19 extension using DNA polymerase across that wide area,

20 a piece of DNA that they can sequence that contains a

21 snip. That's the goal.

22 Q. So after that extension, then, how is this DNA

23 molecule 950 formed between the extended probe and the

24 other probe?

25 A. The extended product is generated, and that's it.

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1 Q. The extended product is attached to both of the
2 original nucleic acid probes; is that correct?

3 A. It's not attached. That would require a covalent
4 bond. That would require a ligase to form that
5 covalent bond. And that is not happening by DNA
6 polymerase.

7 Q. In molecule 950, are there any breaks between segment
8 935 and segment 945?

9 A. What do you mean, are there any breaks?

10 Q. Is molecule 950 a single molecule?

11 A. 950...

12 Q. In step 815.

13 A. That portion is a single molecule. There are breaks,
14 in fact, because there is no covalent bond. There's
15 no ligase to connect them covalently. It's a --
16 that's what it -- that's what it is.

17 Q. So '456 states that "DNA molecule 950 that is formed
18 in the extension/ligation reaction." That's in
19 paragraph 182, and we were just looking at that.

20 In that disclosure, So does not state that
21 there are multiple pieces of molecule -- DNA molecule
22 950. Correct?

23 A. They don't state it, but a person of skill in the art
24 would understand that because there's no ligase.

25 Q. You agree a person of skill in the art would

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1 understand ligation reactions of -- ligation of
2 nucleic acids. Correct?

3 A. A person of skill in the art would understand exactly
4 what a ligation is, the product of a ligation.

5 Q. And the ligation as a product of the ligase, is that a
6 routine laboratory technique used before
7 February 12th, 2018?

8 A. A POSA would understand what it is, and that's why
9 they would know that it's not used here because the
10 only thing that's used here is a DNA probe, and as
11 stated, the patent references "ligate" twice relevant
12 to Figure 9.

13 Q. In Figure 9, we're still looking at step 815, the DNA
14 molecule 950 that is formed, it has, on the left side,
15 segment 935. Correct?

16 A. That's what I see.

17 Q. And it has on the right side, segment 945. Correct?

18 A. That's what I said, yes.

19 Q. All right. And underneath this --

20 A. But they're not linked covalently. They're pieces.

21 Q. Are you finished? Sorry, are you finished?

22 A. I am.

23 Q. So underneath molecule 950 in this figure -- so at
24 step 18 there's another arrow pointing down to the

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next step 820. Do you see that?

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1 A. I do.

2 Q. And what's depicted in step 820 here, in your opinion?

3 A. What's going on between 820 and 825.

4 Q. 820 and the next immediate portion of the figure

5 underneath 820, is that -- is that a thermal --

6 isothermal amplification?

7 A. That's my understanding.

8 Q. And step 820, underneath molecule 950 on the left,

9 there's a small molecule labeled 935A. Do you see

10 that?

11 A. I do.

12 Q. And on the right there's a small molecule labeled

13 945A. Do you see that?

14 A. I do.

15 Q. What is your understanding of what molecules 935A and

16 945A represent?

17 A. I believe they're -- one of them is a primer for the

18 extension which binds to either 935 or 945 because

19 they're reverse complements of each other.

20 Q. And then in the figure underneath that, does that

21 depict a copy of molecule 950? Strike that.

22 The figure underneath the one that we were

23 just looking at, there's two strands represented

24 there. Do you see that?

25 A. I do.

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1 Q. And the top strand has a label 950. Do you see that?

2 A. Right.

3 Q. And then there's a molecule directly underneath it

4 that doesn't -- doesn't appear to have a number label.

5 Do you see that?

6 A. I do.

7 Q. What is this bottom strand in this pair of strands?

8 A. It appears to be a classic Illumina capture sequence

9 for DNA sequencing, but it's got an SBS component at

10 130 and 160 binds to 135. And this is like classic

11 Illumina sequencing.

12 Q. I think you're looking at the wrong molecule. So --

13 it looks like you're looking at capture probe

14 molecule, the very bottom of this figure.

15 A. Uh-huh.

16 Q. I'm going up above.

17 A. Okay.

18 Q. There's a label on the left that says step 825.

19 A. Right.

20 Q. Slightly above that and to the right there's a pair of

21 molecules, horizontal molecules.

22 A. Right.

23 Q. Do you see that?

24 A. I do.

25 Q. And of that pair, the top one has a label 950. Do you

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1 see that?

2 A. I do.

3 Q. And the bottom one does not have a number label on it.

4 Do you see that?

5 A. I do.

6 Q. Okay. So my question to you is, in this pair of

7 molecules, what does the bottom molecule represent?

8 A. It's a copy of the top one.

9 Q. Is that a reverse complement of the top molecule?

10 A. It would be.

11 MR. HOLMAN: Okay, let's take a break, go

12 off the record.

13 (Off the record at 10:07 a.m.)

14 (Back on the record at 10:27 a.m.)

15 MR. HOLMAN: Back on the record.

16 A. I may have misheard you with a company you asked me

17 about. I thought you said Alumina, and you may have

18 asked me about Alluvium. Is that true?

19 BY MR. HOLMAN:

20 Q. That is correct. I was asking you about Alluvium.

21 A. Okay. So I misheard you.

22 Q. Okay. So let me go back to that. So do you have a

23 relationship with a company called Alluvium

24 Biosciences?

25 A. I did, but no longer because that company has been

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1

shut down.

2

Q. What was your relationship with Alluvium?

3

A. I was cofounder.

4

Q. And when did you found Alluvium?

5

A. I think 2009.

6

Q. And when did it shut down?

7

A. Probably like 2015. Maybe a little later.

8

Q. And what type of -- what type of work did Alluvium

9

Biosciences do?

10

A. It was antibiotic drug discovery.

11

Q. Okay. Thanks for clarifying that.

12

A. Thank you.

13

Q. All right, Dr. Sherman, just before the break we were

14

looking at Figure 9 in the '456 reference, so I'd like

15

to continue discussing that figure with you.

16

Step 825 at the bottom of Figure 9 depicts

17

molecule 950 encapsulated on a capture probe on an

18

array; is that correct?

19

A. That's what I see.

20

Q. And this molecule 950 comprises a segment 935; is that

21

right?

22

A. That's right.

23

Q. And also comprises segment 945; is that correct?

24

A. Right.

25

Q. And segment 935 is also present in the original

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1 molecule 950 formed in step 815. Correct?

2 A. 935 is found in the original.

3 Q. And same question for 945, it was also present in the

4 original molecule 950. Correct?

5 A. Right. The -- but this is a copy of that.

6 Q. All right. Let's look at the capture probe part of

7 this figure at the bottom of Figure 9. The capture

8 probe here has four labeled segments. Do you see

9 that?

10 A. I do.

11 Q. And in your opinion in your declaration, you believe

12 that segment 130 is an SBS primer region; is that

13 correct?

14 A. That is correct. It's an SBS region.

15 Q. All right. How about segment 960 of the capture

16 probe, what is that?

17 A. Based on the figure, it's a complement to the copy

18 form of 935.

19 Q. Would you call that a capture region of the probe?

20 A. That would be an appropriate...

21 Q. How about segment --

22 A. I didn't finish. Hold on, please.

23 Right, that's the capture region, 960.

24 Q. All right. And then on the captured molecule 950,

25 what is segment 945?

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1 A. I would like to just check that. It's an SBS primer
2 region.

3 Q. Okay. If segment 130 encapture probe is an SBS primer
4 region and segment 945 encaptured molecule 950 is the
5 other SBS primer region, what segments of the molecule
6 would be present in the sequencing product?

7 A. Well, because the way we see it here now in Figure 9,
8 we can surmise that the top is 5 prime, the bottom is
9 3 prime, and the chain synthesis by DNA polymerase
10 would go up and would extend through the 950 region
11 to 945, so that would be included, that new part
12 which would be from the classic Illumina DNA
13 sequencing unit directional sequencing.

14 Q. So that would include segment 960; is that right?

15 A. Well, it would extend just above 60 up through 945.

16 Q. Okay, but what -- what segments end up being sequenced
17 from the Illumina sequencing, for example?

18 A. 950 through 945.

19 Q. Okay. So segment 125 would not be part of that
20 sequencing; is that correct?

21 A. That's correct.

22 Q. Before February 12th, 2018, would a person of ordinary
23 skill in the art have understood what an FFPE tissue
24 sample is?

25 A. ^{www.LexitasLegal.com/Premier} They would have been familiar with that from in situ ^{Lexitas}

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1

hybridization.

2

Q. What would -- what's a person of ordinary skill in the
art's understanding of FFPE tissue sample?

3

4

A. It's a formal and fixed paraffin-embedded tissue
sample.

5

6

Q. What are the reasons that someone might use a FFPE
tissue sample in their research?

7

8

A. For in situ hybridization to essentially immobilize
the tissue sample for in situ hybridization.

9

10

Q. And was using FFPE tissue samples to immobilize the
sample for in situ hybridization, was that routinely
done before February of 2018?

11

12

13

A. Preparing the samples, yes.

14

15

Q. Was in situ hybridization in FFPE tissue samples
routinely done before February 2018?

16

17

A. Just standard straightforward in situ hybridization,
single probe in situ hybridization, was known.

18

19

Q. How about a fresh tissue sample? How is a fresh
tissue sample different from an FFPE tissue sample?

20

21

A. An FFPE is embedded in paraffin and a fresh sample
would not be.

22

23

Q. So what reasons would a POSA have to use a fresh
tissue sample instead of an FFPE tissue sample?

24

A. There could be some unwanted effects of the embedding

25

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process and fixing process that could change

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1 potentially, could change the nature of the sample.

2 Q. What are some examples of unwanted effects?

3 A. There could be chemical processes that may change
4 some aspects of the tissue sample; either, you know,
5 in the tissue itself, you know, oxidation of
6 molecules in the cell also. So it could just change
7 the nature of the sample; be, perhaps, less authentic
8 compared to -- could -- not necessarily, but could be
9 less authentic than a fresh frozen sample.

10 Q. So based on the user's interest that the POSA might
11 use -- might select an FFPE sample or they might
12 select a fresh frozen tissue sample depending on the
13 research that they were doing; is that correct?

14 A. I think that's reasonable.

15 Q. You mentioned "fresh frozen." Is there a difference
16 between a fresh tissue sample and a fresh frozen
17 tissue sample?

18 A. A fresh versus fresh frozen?

19 Q. Yes.

20 A. Yeah, there is. In terms of -- you mean, one's
21 frozen and one isn't. Right?

22 Q. Right. So what are the reasons a POSA might use a
23 fresh frozen tissue sample as opposed to a fresh
24 tissue sample or FFPE tissue sample?

25 A. Fresh frozen if, for example, you need to preserve

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1 the sample for processing. You know, you have many
2 samples that you need to process it, it simply
3 wouldn't be practical to process 100 samples within a
4 certain timeframe because if they're fresh, the ones
5 that you process later are probably going to be a
6 little different than the ones that you process
7 earlier. So you sort of freeze it in time. You can
8 process them. They're frozen at that time. So that
9 would be a difference.

10 Q. All right. Do you still have the '689 patent in front
11 of you?

12 A. I do.

13 Q. Could you turn, please, to column 41 of the '689
14 patent? And let me know once you're there.

15 A. Okay. I'm there.

16 Q. All right. And I'll direct your attention to the
17 bottom of this column, beginning at line 66. And,
18 there, the '689 patent discloses, quote, "Compositions
19 and kits of the present disclosure can include probes
20 and other reagents, for example, buffers and other
21 reagents known in the art to facilitate binding of a
22 protein and/or nucleic acid in a sample, i.e., for
23 performing hybridization reactions."

24 Did I read that correctly?

25 A. Yes.
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1 Q. Do you agree with the '689 patent, that buffers and
2 other reagents were known in the art to facilitate
3 binding of nucleic acids in hybridization reactions?
4 A. I agree with that statement in its particular context
5 or set the stage in this specification.
6 Q. In what routine ways would a POSA have treated an FFPE
7 tissue sample in order to facilitate binding of
8 nucleic acid probes to a target analyte in that tissue
9 sample?
10 A. They would have known or there would have been
11 literature on, you know, the basics, how you create
12 the sample, what sort of buffers you use, what sort
13 of -- you know, how to maintain that sample in a form
14 that would be stable and represent what you're
15 interested in eventually investigating.
16 Q. What is a -- what is one specific way a POSA would
17 have treated an FFPE tissue sample in order to
18 facilitate binding of nucleic acid probes to target
19 analyte?
20 A. To adhere to best practices for handling those
21 samples to avoid any disruption of nucleic acids.
22 Q. That sounds like a reason to treat the tissue sample.
23 I'm asking you specifically what a POSA would have
24 done to treat the FFPE tissue sample? Can you provide
25 me with a specific way in which a POSA would have

1 treated FFPE tissue sample?

2 A. There are steps in terms of buffers that are used,
3 you know, sort of buffers to use ahead of time,
4 buffers to use during, buffers to use after, which
5 would be standard for in situ hybridization.

6 Q. All right. How about a fresh frozen tissue sample?
7 What routine ways would a POSA treat a fresh frozen
8 tissue sample to facilitate binding of nucleic acids
9 to a target analyte?

10 A. There would be a set of best practices for handling
11 that type of tissue sample to maintain its integrity
12 in terms of buffers and timing and pH. Those types
13 of parameters would be followed.

14 Q. Can you name specifically a way in which a POSA might
15 have treated fresh frozen tissue sample in order to
16 facilitate binding of nucleic acids to a target
17 analyte?

18 A. They would treat with a particular buffer that would
19 enable a probe to potentially bind.

20 Q. Earlier, you said there's a set of best practices for
21 handling that type of tissue sample. Are there best
22 practices for handling fresh frozen tissue samples and
23 best practices for handling FFPE tissue samples?

24 A. I believe so for standard manipulations, not for
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specialized or advanced or multiplexed. That's a

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1 whole different matter, which is provided in this
2 specification.

3 Q. Provided in the specification, are you referring to
4 the buffers and other reagents known in the art to
5 facilitate binding of a protein and/or nucleic acid in
6 a sample for performing hybridization reactions?

7 A. No. Those are just the most, you know, basic
8 high-level statements. You know, there are specific
9 examples about how to treat -- how to actually treat
10 the sample when you have a multiplexed system for
11 hybridizing probes to a sample.

12 Q. Would you agree that the patent discloses here, the
13 section we're looking at, compositions and kits of the
14 present disclosure can include these buffers and
15 reagents known in the art? Correct?

16 A. I mean, that's just like a broad statement that sets
17 up the specification.

18 Q. Okay. What's the specific example of treating tissue
19 sample that you're referring to in the '689 patent?

20 A. I'll have to find it. So if you go to column 40,
21 line 4, I'm happy to read that, or... but this is the
22 place in the specification that provides critical
23 constructions as to how it actually used -- developed
24 and used probe concentrations that are lower than

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25 what is typical for immunohistochemistry and in situ

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1 hybridization, so that from 4 to 20 lays out those
2 details which are details that are important
3 teachings in the specification.

4 Q. Okay. But that's referring to concentrations of the
5 probes. Correct?

6 A. Exactly. Yes.

7 Q. How does the concentration of a probe treat the tissue
8 sample to facilitate binding?

9 A. Well, that's what makes this unique in terms of, you
10 prepare the tissue sample and, in order for the
11 experiment to work, it provides guidance in terms of
12 the probe concentrations.

13 Q. How do you prepare the tissue sample for this
14 embodiment?

15 A. So the protocol is found in Figure 21B.

16 Q. Okay. In what part of Figure 21B is the tissue sample
17 treated to facilitate binding of nucleic acid probes
18 to a target analyte?

19 A. Well, there are three examples, 7, 8, and 9 that
20 provide the details on how these samples are handled.

21 Q. Are you referring to Figure 21B?

22 A. Right.

23 Q. You said there's three examples, 7, 8, and 9.

24 A. 7, 8, and 9.

25 Q. ^{www.LexitasLegal.com/Premier} What are you referring to, ^{Lexitas} examples 7, 8, and 9 in

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1

Figure 21B?

2

A. So column 75 is Example 7, and column 77 has

3

Example 8 and 9.

4

Q. All right. And in Example 7, where is the -- where

5

does it disclose treating the tissue sample in order

6

to facilitate binding nucleic acid probes?

7

A. Well, it explains an example of how these probes,

8

different probes, were used; what the probes are made

9

up of; regions of interest; and it names the type of

10

target. And so, for 7, it's target proteins and

11

target R&As. For 20, they prepare a 5 micron FFP

12

section. And in Example 9, they prepare a 5 micron

13

section as well.

14

Q. Okay. But how is that 5 micron section, let's say,

15

for example, 9, how is that 5 micron section treated

16

in order to facilitate binding of these probes to

17

target analyte?

18

A. Well, they -- as I've said, they provide guidance on

19

how to treat the sample with lower concentrations of

20

probes than would normally be used in in situ

21

hybridization.

22

Q. So are you saying that by adding lower concentrations

23

of probes, you're treating the sample to facilitate

24

binding?

25

A. Well, the sample is prepared as would be known to a

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1 person of skill in the art. I mean, that's what's
2 stated in the patent, as we read.

3 Q. Okay. So is --

4 A. Now, going to the next step, they lay out unique
5 procedures.

6 Q. And by "unique procedures," you're referring to the
7 disclosed concentrations of the probes that are used.

8 A. That's right.

9 Q. Okay. All right. In the '689 patent, let's take a
10 look at column 30. And I want to specifically look at
11 column 30, line -- beginning at line 59 where the
12 patent refers to a gap extension -- basically lines 59
13 through 65. You can just read that to yourself.

14 A. All right.

15 Q. Okay. And so here the '689 patent discloses that when
16 "the first and the second nucleic acid probes are not
17 adjacent and not overlapping, the method comprises
18 performing a gap extension and a nick repair reaction
19 such that the first and second nucleic acid probes are
20 ligated together."

21 Is that right?

22 A. That's correct.

23 Q. Okay. How would a POSA perform the gap extension
24 that's disclosed here?

25 A. So gap extension could be done with a polymerase and

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1 -- to connect the two, and then the ligase to create
2 the covalent bond.

3 Q. And when you say polymerase "to connect the two," are
4 you referring to the two probes?

5 A. That's right.

6 Q. Okay. And which -- are both probes extended by the
7 polymerase?

8 A. One probe.

9 Q. Okay.

10 A. It's unidirectional.

11 Q. So one probe is extended out of the polymerase towards
12 the other probe, and then the patent discloses there's
13 a nick repair reaction.

14 A. Right.

15 Q. How does -- how does that work?

16 A. Well, if you have -- if you look through the patent,
17 specifically, gas enzymes are noted numerous times.
18 In particular, T4 ligase appears numerous times in
19 the patent, and T4 ligase is what will catalyze the
20 ligation reaction which is a covalent bond formation,
21 and those are -- those are then formally chemically
22 linked to one another.

23 Q. Is that -- so is nick repair separate from the
24 ligation itself?

25 A. Nick repair and -- nick repair includes the ligation

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reaction.

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2 Q. Okay.

3 A. The ligase. Yeah.

4 Q. And you said an example is the T4 ligase --

5 A. Right.

6 Q. -- right?

7 And was T4 ligase known in the art before
8 February 12th of 2018?

9 A. How to conduct a normal ligation reaction by a ligase
10 that involves catalyzing the covalent bond would have
11 been understood by a person of skill in the art, so
12 this would have been understood by a person of skill
13 in the art to involve in a formal ligation reaction
14 to catalyze by a ligase.

15 Q. And how do you know it was catalyzed by a ligase here?

16 A. The patent has numerous places where T4 ligase is
17 noted.

18 Q. Before February 12, 2018, would a POSA have understood
19 what denaturation is in the context of two nucleic
20 acid strands that are hybridized together?

21 A. Yes, that -- a POSA would have understood that in the
22 context of their training in molecular biology.

23 Q. And what would a POSA's understanding of denaturation
24 be?

25 A. That a double-stranded DNA can be separated into

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1 individual single strands by certain types of
2 treatments. And that's called denaturation.

3 Q. And what are examples of certain types of treatments
4 that would -- that a POSA would have known to denature
5 nucleic acid strands?

6 A. So one common method that a POSA would have
7 understood at that time is elevated temperature can
8 separate the strands into two individual strands.
9 Another approach would be to increase salt
10 concentration to advance the same effect; to take a
11 double-stranded DNA, separate it into two individual
12 strands.

13 Q. What factors impact the efficiency of denaturing two
14 nucleic acid strands?

15 A. There are various physical chemical parameters in
16 terms of -- that control the binding, the strength of
17 the hybridization. Depends on the sequence. It
18 depends on if it's 100 percent homologous. So
19 there's a perfect match or maybe there's an imperfect
20 match. In the middle, on one end or the other or
21 more than one mismatch, that can -- among others,
22 that can affect the conditions he used.

23 Q. If two nucleic acid strands are, as you said,
24 100 percent homologous, a perfect match, would that
25 require more stringent denaturing conditions compared

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1 to two strands that are not 100 percent homologous
2 perfect match?

3 A. Generally, that -- a POSA would understand that with
4 a perfect match the conditions to denature are
5 usually more stronger conditions, higher temperature,
6 more salt.

7 Q. Okay.

8 A. Stringency is -- means something a little different
9 to me, that's why I didn't use that term the way you
10 did. But I know what you mean, and the answer is,
11 for a perfect match generally it depends on the
12 sequence of girth [ph], the length of it, the type of
13 base pairing; you know, the types of bases that are
14 involved. Are they all GCs? Just a long strand of
15 GCs or ATs or is it mixed up? So it really does
16 depend on the circumstance. But in general, if it's
17 a perfect match in order to get them apart, you need
18 more severe conditions.

19 Q. And I think you mentioned temperature, so we'll use
20 that as an example. So perfect match, two nucleic
21 acid strands that are a perfect match, would those
22 require a higher temperature to denature them than two
23 strands that are not perfectly matched?

24 A. Generally. Again, it would depend on the nature of
25 the sequences that you compare.

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1 Q. Would the same principle apply for salt concentration?

2 A. I would say, in general, the same provisos would

3 apply in terms of the nature of the sequence, the

4 length of it, the types of bases in the sequence; the

5 length, types of bases. But in general a POSA would

6 understand that for a perfect match, a higher salt

7 concentration would be required to separate the

8 double strand into two single strands.

9 Q. All right. In your declaration, Dr. Sherman, you

10 provide opinions on the '487 application, which is

11 Exhibit 1009. Correct?

12 A. That's correct.

13 Q. And in particular, you provide some opinions about the

14 '487 application's disclosure of a negative

15 purification method. Do you recall that?

16 A. I do.

17 Q. Before February 12th, 2018, would a POSA have

18 understood the term "negative purification"?

19 A. I mean, I found that term a little unusual, but, you

20 know, once you kind of look into the term and its

21 meaning, a POSA would have followed that language.

22 Q. What would -- generally, what would the POSA's

23 understanding of the term "negative purification" be?

24 A. To remove some sort of analyte from a mixture.

25 Q. All right. In your declaration -- actually, I'm going

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1 to hand -- I'm going to give you another exhibit.

2 I'll give you a copy of the '487 application.

3 MR. HOLMAN: So this is marked as
4 Exhibit 1009.

5 ENTERED INTO THE RECORD:

6 PREVIOUSLY MARKED EXHIBIT 1009

7 11:15 a.m.

8 BY MR. HOLMAN:

9 Q. And, Dr. Sherman, you recognize this document as the
10 '487 application?

11 A. Yes.

12 Q. If you please turn to page 56, paragraph 252 in this
13 document.

14 A. Okay.

15 Q. You provide an opinion of this paragraph in your
16 declaration. Correct?

17 A. I did.

18 Q. Now, here in paragraph 252, the '487 application
19 discloses that "Background noise, during nucleic acid
20 detection, can be reduced by performing a negative
21 purification of the intact probe molecule."

22 Do you see that sentence there?

23 A. I do. Right.

24 Q. And do you agree that this is a disclosure stating
25 that background noise can be reduced by pulling out

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1 the intake probe molecule?

2 A. Yes, I agree.

3 Q. All right. You can put that aside. If you go back to
4 your declaration, paragraph -- I want to look at
5 paragraph 96, please.

6 A. Okay.

7 Q. All right. Here you state, in the second sentence
8 there, the bottom of page 52, paragraph 96, you state,
9 "It is my understanding that U.S. Patent Application
10 Number 14/946,386 is incorporated by reference into
11 the '487 application."

12 Do you see that testimony there?

13 A. I do. I see it, yes.

14 Q. What is the basis for your understanding that you
15 stated here?

16 A. It's specifically cited in the '487 application.

17 Q. Do you have an understanding of the legal requirements
18 for incorporation by reference?

19 A. I mean, I'm not a lawyer, but counsel did state that
20 it is incorporated by reference into the '487.

21 Q. Did you assess whether this document is, in fact,
22 incorporated by reference?

23 A. I was informed by counsel that it was, and I treated
24 it as such.

25 Q. All right. If you could now flip in your declaration

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1 over to paragraph 110, please. It's on page 65.

2 All right. And here in your second
3 sentence you state, "U.S. Patent Application
4 Publication Number 2010/0015607 is a reference that is
5 entirely incorporated by reference into '487
6 application."

7 Do you see that testimony?

8 A. I do.

9 Q. Okay. And what's the basis of your statement that
10 this one is incorporated by reference?

11 A. I was informed by counsel that this application that
12 you noted, 2010/0015607, is incorporated by reference
13 to the '487 application.

14 Q. All right. In the next paragraph, 111 of your
15 declaration, you refer to this '607 publication as
16 disclosing probe pairs "that can hybridize to a target
17 nucleic" acid.

18 Is that correct?

19 A. That's exactly what I state here, yes.

20 Q. It looks like there's maybe a word missing in that
21 first sentence. You state, "probe pair that can
22 hybridize to target nucleic." Should that be nucleic
23 acid?

24 A. Yes, it should.

25 Q. And then on the next page of your declaration you

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1 provide a copy of Figure 1A and 1C of the '607

2 publication. Do you see that?

3 A. I see it, yes.

4 Q. And is it your opinion that this figure discloses
5 probe pairs that can hybridize to a target nucleic
6 acid?

7 A. Yes.

8 Q. Okay. And then on the next page of your declaration,
9 paragraph 112, you testified that a POSA would have
10 understood that a probe pair can indirectly hybridize
11 to a target nucleic acid via an indirect target
12 binding domain.

13 And then you provide -- you state that an
14 example is depicted -- an example of this concept is
15 depicted in Figure 14, and you have a copy of the '487
16 application's Figure 14 there. Is that -- is that
17 right?

18 A. That is correct.

19 Q. Okay. So in this Figure 14, where is the probe pair
20 that you're referring to?

21 A. Well, in this particular example, the probe pair is
22 that intermediary oligonucleotide where one is
23 hybridized specifically to the target nucleic acid
24 and the other part of that pair binds to the target

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binding domain.

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1 Q. So are you saying that the intermediary
2 oligonucleotide depicted here in Figure 14 is a
3 pair -- that alone is a pair of probes?
4 A. Well, it is. I mean, one part of the pair hybridizes
5 to the target and the other part hybridizes the
6 target binding domain. They're two distinct regions.
7 Q. But isn't that the same -- all the same molecule? Is
8 it not one probe?
9 A. But it's a pair of sequences that have a different
10 function.
11 Q. So in your opinion, a pair of probes can be defined as
12 a pair of sequences that have different function?
13 A. In this particular case, yes.
14 MR. HOLMAN: All right, let's take a break.
15 Let's go off the record.
16 (Off the record at 11:26 a.m.)
17 (Back on the record at 11:26 a.m.)
18 BY MR. HOLMAN:
19 Q. A few more questions. Do you agree that the '487
20 application describes the intermediary oligonucleotide
21 of Figure 14 as a probe?
22 A. I would have to look exactly where that word usage
23 is. Do you -- can you point to it or...
24 Q. I can direct you to it.
25 A. Thank you.

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1 Q. All right. If you could -- in the '487 application,
2 if you could turn to paragraph 233. It's on page 52.
3 A. Okay.
4 Q. And this paragraph refers to Figure 14. Do you see
5 that?
6 A. I see it.
7 Q. And then six lines down there's a sentence in this
8 paragraph that reads, quote, "It could be said that
9 the intermediary oligonucleotide acid is a probe, as
10 comprised herein, since it comprises a nucleic acid
11 backbone and is capable of binding a targeted nucleic
12 acid," end quote.
13 Do you see that sentence?
14 A. I do.
15 Q. So do you agree that the '487 application states that
16 the intermediary oligonucleotide can be a probe as
17 defined herein?
18 A. It says it's a probe. The probe has a pair of
19 hybridizing regions that are different, and therefore
20 it's a probe pair.
21 Q. It doesn't say -- it doesn't use those words, "probe
22 pair," does it?
23 A. It uses the word "probe." It certainly nowhere
24 excludes the point that there could be a pair of
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hybridizing sequences, which is what this

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1 intermediary oligonucleotide has. So you look at
2 that and you realize a POSA would realize that it's a
3 probe pair by virtue of the fact that it hybridizes
4 to a target nucleic acid, on the one hand, one
5 region, and the second member of that pair binds the
6 target binding domain, just as we see in Figure 14.

7 It's -- I think the visual shows it nicely.

8 Q. Are you using the term "probe pair" synonymously with
9 "pair of probes"?

10 A. Well, it's a -- it is a probe pair. It has two
11 regions that hybridizes to distinct targets.

12 Q. So in your opinion, a probe pair can be a single
13 molecule or two separate molecules; is that correct?

14 A. Well, in this instance it's a -- it's a single
15 intermediary probe with two portions that comprise
16 distinct regions for hybridization, so it's a probe
17 pair.

18 Q. And in the Figure 1A to 1C of the '607 publication --

19 A. Excuse me, let me just go there. What page is that?

20 Q. That's on your declaration page 66.

21 A. Thank you.

22 Q. So in this figure, the probe pair comprises two
23 separate molecules. Correct?

24 A. In this particular case. It's a direct probe.

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There's no intermediary probe. That comprises a pair

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1 of hybridizing sequences.

2 Q. So are you saying that a POSA would read this '607
3 publication and see two separate probes binding a
4 target nucleic acid, and take from that that they
5 could interpret a single intermediary oligonucleotide
6 as a pair of probes?

7 A. Well, a POSA doesn't need this to interpret that. A
8 POSA can look at it and interpret the meaning of it
9 because it's clearly revealed in Figure 14.

10 Q. If this intermediary oligonucleotide is a pair of
11 probes or a probe pair, as you've said, is it
12 subsequently ligated to another probe?

13 A. In this case, there is no need for that.

14 Q. So this would be a -- in your view, this is a probe
15 pair that's not ligated together after binding the
16 target nucleic acid?

17 A. There's no need for it because the probe pair, as you
18 see, is -- comprises this intermediary
19 oligonucleotide with two hybridizing regions, so
20 there's no need for a ligase or a ligation.

21 Q. So this embodiment you're referring to is irrespective
22 of your discussion of probe ligation in your
23 declaration.

24 A. Well, a POSA would look at this and be able to
25 distinguish the direct binding to a target with

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1 distinct probes as a probe pair that could be ligated
2 with a ligase to form a single contiguous fragment
3 versus what we see in Figure 14 which the probe pair
4 is encompassed on this intermediary oligonucleotide.
5 And by virtue of its hybridization to two distinct
6 targets, it's a probe pair.

7 Q. So would you agree that in this figure, as an
8 intermediate -- that discloses this intermediary
9 oligonucleotide as a probe pair, as you've said, this
10 is not a disclosure of ligating probe pairs?

11 A. Correct. In this case, there's no need for that.

12 Q. All right. In your declaration, if we could turn a
13 few pages to paragraph 117. It's on page 70.

14 A. Right.

15 Q. All right. And in the second sentence here you state,
16 "In U.S. Patent Application Publication Number
17 2011/0086774, which I have been informed is entirely
18 incorporated by reference, a first oligonucleotide and
19 a second oligonucleotide both hybridize to a third
20 oligonucleotide called a 'bridging oligo.'"

21 Do you see that testimony there?

22 A. I do.

23 Q. And similar question as I asked you before, what's the
24 basis for understanding that this '774 publication is
25 incorporated by reference in the '487 application?

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1 A. I was informed by counsel that Publication Number
2 2011/008677 is incorporated by reference to the '487
3 application.
4 Q. All right. And then in this discussion of the '774
5 publication, you provide a copy of Figure 8A of the
6 '774 publication; is that right?
7 A. I see Figure 8 at the top. You're talking about the
8 bottom of page 70?
9 Q. Correct. The figure you provide --
10 A. Oh, I -- sorry. I see the 8 over at the left. I see
11 it.
12 Q. Okay. So I'm going to hand you a copy of the '774
13 publication.
14 MR. HOLMAN: So this is marked as
15 Exhibit 2010.
16 ENTERED INTO THE RECORD:
17 PREVIOUSLY MARKED EXHIBIT 2010
18 11:40 a.m.
19 A. Thank you.
20 BY MR. HOLMAN:
21 Q. All right. And, Dr. Sherman, you recognize this as
22 the '774 publication that you discuss in your
23 declaration?
24 A. I do.
25 Q. All right. And if you could turn to Figure 8 of this

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1 document. It's on page 9 of your -- of the reference.

2 And that's Figure 8, the same figure that you provide

3 in your declaration. Correct?

4 A. Right.

5 Q. All right. If you could turn to paragraph 83 in the

6 '774 publication. That's going to be on page 9.

7 Sorry, page 26. I'm confusing the bottom page

8 numbers.

9 A. So this is page 9 of 774, and at the bottom it's

10 2010.026?

11 Q. Correct.

12 A. Okay.

13 Q. And I want to look at paragraph 83 on the left-hand

14 column there.

15 A. 83. Sure.

16 Q. All right. Now -- and this paragraph discusses

17 Figure 8 there. Do you see that?

18 A. I do.

19 Q. And four lines down, the '774 publication discloses

20 that "In step 1) of Figure 8 probes containing the

21 oligos are designed to bind pairwise to a target

22 protein and to form a signal oligo by ligation when

23 the probes are brought in proximity."

24 Do you see that?

25 A. I do.

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1 Q. Okay. So here this disclosure is referring to

2 antibody probes -- two -- a pair of antibody probes

3 that bind the same protein target; is that correct?

4 A. Yes.

5 Q. All right. And then the next paragraph, 84, discloses

6 that -- discloses "A bridging oligo comprises a

7 polynucleotide sequence. The oligos attached to the

8 protein probes comprise a portion that is

9 complementary to the bridging oligo."

10 Do you see that disclosure there in 84?

11 A. I do.

12 Q. Now, is this referring to adding a third

13 oligonucleotide called a bridging oligo to the system?

14 A. I mean, I don't -- I don't see -- I don't see the

15 word "third" anywhere. It's called a bridging oligo.

16 It's a bridging oligo.

17 Q. Okay. Well, if you look in your declaration,

18 paragraph 117, you state that -- referring to this

19 figure -- "a first oligonucleotide and the second

20 oligonucleotide both hybridize to a third

21 oligonucleotide called a 'bridging oligo'."

22 A. I do state that.

23 Q. So is it fair to say that this bridging oligo -- in

24 your opinion, this bridging oligo is a third

25 oligonucleotide that's added to this system?

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1 A. I mean, in terms of -- yes, that's what I state.

2 Q. Okay. And in the next step -- going back to the '774

3 publication, in the next step, paragraph 85 refers to

4 step 4 and states that "the components required for

5 probe ligation are added."

6 Do you see that?

7 A. Yes.

8 Q. And so would this be adding a ligase enzyme to ligate

9 the first and second oligos that were conjugated to

10 the antibody probes?

11 A. Yes.

12 Q. All right. And then just a few more questions. We're

13 almost done and we can break for lunch.

14 The next paragraph of '774 publication,

15 paragraph 86, refers to step 5 of Figure 8, and it

16 states that, "After ligation, the signal oligo is then

17 released via disulfide reduction, uracil excision,

18 restriction digest, proteinase K, or any other

19 suitable method known in the art."

20 Do you see that?

21 A. I do.

22 Q. And so here, after the ligation, the '774 publication

23 discloses that the single oligo is released. Correct?

24 A. I see that. I also see up above, just to be clear,

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the ligation reaction. There is specific ligases

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1 noted in that paragraph 85. That tells me that it's
2 the kind of ligase that generates a covalent bond.

3 Q. All right. Now, if you could turn to figure -- go
4 back to Figure 8 of the '774 publication. Now I'm
5 going to direct your attention to Figure 8C, which is
6 not in your declaration, so I think you need to turn
7 to the actual exhibit.

8 A. Okay. I'm there.

9 Q. All right. Figure 8C, step 6 refers to -- or
10 discloses releasing the oligo there; is that correct?

11 A. I'm sorry, but that was paragraph 86? Is that what
12 you were looking at? Yeah.

13 The single oligo is then released from
14 paragraph 86. I believe that's what you were asking.

15 Q. Yeah. Thank you.

16 MR. HOLMAN: All right, let's stop there
17 and go off the record.

18 (Off the record at 11:49 a.m.)

19 (Back on the record at 12:33 p.m.)

20 MR. HOLMAN: Okay, Dr. Sherman, welcome
21 back.

22 BY MR. HOLMAN:

23 Q. During the course of this deposition today, during any
24 of the breaks, did you speak to anyone?

25 A. No.

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1 MR. HOLMAN: All right, Dr. Sherman. Thank

2 you for your time. We have no further questions for
3 you. We'll pass the witness, subject to any redirect.

4 MR. WALTER: I have a few questions.

5 EXAMINATION

6 BY MR. WALTER:

7 Q. If you can go to Exhibit 1001 and go back to column
8 30.

9 MR. WALTER: For the record, Exhibit 1001
10 is the '689 patent.

11 A. 1001 --

12 BY MR. WALTER:

13 Q. Column 30.

14 A. -- 30, thanks. All right.

15 Q. And do you recall earlier during your direct
16 examination you were asked some questions about the
17 passage that appears at column 30, lines 59 to 65?

18 A. Yes.

19 Q. And in particular, you were asked about the last
20 clause that refers to performing a gap extension, a
21 nick repair --

22 A. Right.

23 Q. -- such as the first and the second nucleic acid
24 probes are ligated together.

25 A. Right.

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1 Q. Do you see that?

2 A. Right. I do.

3 Q. Can you briefly explain how in your opinion this

4 disclosure is different from the disclosure that

5 appears in Figure 9 of So '456?

6 MR. HOLMAN: Objection. Leading.

7 A. This specifically describes a formal ligation with --

8 in a process that involves the formation of a

9 covalent bond, which is the essence of a ligase

10 enzyme, and that nick repair reaction would include a

11 ligase and formation of that covalent bond.

12 BY MR. HOLMAN:

13 Q. Okay. And let's go to So '456, Figure 9. That's

14 Exhibit 1005.

15 A. Yep. Okay.

16 Q. And you can see there is a figure that looks kind of

17 like a star and it's identified with number 915.

18 A. Correct.

19 Q. What is your understanding of what that is?

20 A. That's a mutation, otherwise known as a snip. So

21 it's a sequence of interest.

22 Q. Now, considering that depiction of a snip and, as you

23 refer to it as a sequence of interest in Figure 9,

24 does that, in your opinion, relate to any other

25 www.LexitasLegal.com/Premier Lexitas differences between the reaction that's described in

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1 column 30 of the '689 patent and Figure 9 of So '456?

2 MR. HOLMAN: Objection. Form.

3 A. Column 30 of the '689?

4 BY MR. WALTER:

5 Q. Yes, the one we looked at just a moment ago.

6 A. Ah. Right. I mean, the purpose of this is to,
7 essentially, use sequence by synthesis to gain access
8 to that sequence of interest, and then using, you
9 know, the typical Illumina technology to obtain the
10 DNA sequence for that, sort of the nucleic acid
11 sequence across that region of interest. There's an
12 extension reaction, there's no ligation involved, so
13 it's distinguished clearly from the '689 column 30,
14 that segment of lines 59 to 65.

15 Q. Do you see in Figure 9 there's a gap between those two
16 probes that includes the sequence of interest 915
17 in-between?

18 A. A gap. Like right -- you mean at 920?

19 Q. It's in -- it's in 820, and it's also in 810.

20 A. 820. I do see that gap.

21 Q. What's your understanding of how that gap compares to
22 the gap that is potentially in figure -- in column 30
23 of the '689 application. '689 patent. Sorry.

24 A. I mean, visually, Figure 9, you can see that it's a

25 ^{www.LexitasLegal.com/Premier} large gap. ^{Lexitas} I mean, it's a region that needs to be

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1 extended through a evidently large region. These
2 probes aren't adjacent to each other. There's got to
3 be an extension, you know, whereas here, in column 30
4 of the '689, it states that the nucleic acid probes
5 on the one end are not adjacent and not overlapping,
6 but you can use this gap extension which is then
7 closed with a formal ligation by a ligase enzyme.

8 MR. WALTER: All right, I don't have any
9 further questions.

10 MR. HOLMAN: We have no questions. The
11 deposition is over. Go off the record.

12 (Proceedings concluded at 12:39 p.m.)
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CERTIFICATE OF NOTARY

STATE OF MICHIGAN)

) SS

COUNTY OF OAKLAND)

I, ALISON WEBSTER, certify that this
deposition was taken before me on the date
hereinbefore set forth; that the foregoing
questions and answers were recorded by me
stenographically and reduced to computer
transcription; that this is a true, full and
correct transcript of my stenographic notes so
taken; and that I am not related to, nor of counsel
to, either party nor interested in the event of
this cause.

Alison Webster

ALISON C. WEBSTER, CSR-6266, RPR, RMR, CRR, RDR
Notary Public,
Oakland County, Michigan

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My Commission expires: May 1, 2029

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