

UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT TRIAL AND APPEAL BOARD

GUARDANT HEALTH, INC.,)

)

Petitioner,)

)

vs.)

Case No.

)

IPR2022-00817

UNIVERSITY OF WASHINGTON)

)

THROUGH ITS CENTER FOR)

COMMERCIALIZATION,)

)

Patent Owner.)

)

U.S. Patent No.)

)

10,760,127)

)

March 21, 2023

9:06 a.m.

Deposition of RAHUL SATIJA, held at the
offices of Covington & Burling LLP, 620 Eighth
Avenue, New York, New York, before Laurie A.
Collins, a Registered Professional Reporter
and Notary Public of the State of New York.

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1 R A H U L S A T I J A ,

2 called as a witness, having been duly sworn
3 by the notary public, was examined and
4 testified as follows:

5 EXAMINATION BY

6 ATTORNEY ROSATO:

7 Q. Good morning, Dr. Satija.

8 A. Good morning.

9 Q. Have you sat for a deposition before?

10 A. Yes, I have.

11 Q. Okay. So I'm sure you're familiar with
12 how things work in depositions, but we'll go over
13 a few of the basics, if that's okay with you.

14 A. Of course.

15 Q. Is there any reason you can't provide
16 complete and accurate testimony today?

17 A. No.

18 Q. And as we go through the discussion, I
19 will try to make my questions clear. And
20 likewise, please speak up, make your answers
21 clear. If there is anything you don't understand
22 in a question, I'd ask that you direct your
23 questions to me. Is that okay?

24 A. Of course.

25 Q. Great.

1 And of course -- I'm sure you've heard
2 this before -- verbal answers rather than shaking
3 or nodding your head. It's really hard for the
4 court reporter to pick that stuff up. Okay?

5 A. Okay.

6 Q. Finally, if you want to take a break at
7 any time, we can do that. I just ask if there's a
8 question pending we answer the question before
9 taking a break. Okay?

10 A. I understand.

11 Q. Great.

12 Are you being compensated for your
13 testimony today?

14 A. Yes, I am being compensated for my
15 testimony today.

16 Q. And I should say are you being
17 compensated for your testimony in this proceeding
18 in general.

19 A. Yes, I am being compensated for my work
20 in this proceeding.

21 Q. Who's providing that compensation?

22 A. So, as I say in my declaration, I have
23 been retained on behalf of the University of
24 Washington. But I should say that my compensation
25 is not dependent upon my opinions, my testimony,

1 or the outcome of this case.

2 Q. My question is who's providing your
3 compensation for this proceeding.

4 A. So I know that I've been retained on
5 behalf of the University of Washington. I submit
6 invoices not directly to the University of
7 Washington but to counsel, but the exact details
8 of where the compensation comes from I wouldn't be
9 a hundred percent certain.

10 Q. Okay. So you don't know who's paying
11 you ultimately?

12 A. So I've been retained on behalf of the
13 University of Washington through its center for
14 commercialization. And when I submit my invoices,
15 I submit them to Sterne Kessler.

16 Q. Okay. And are you being paid at an
17 hourly rate?

18 A. Yes.

19 Q. And is all your compensation for this
20 matter being paid at that hourly rate?

21 A. Yes, it is.

22 Q. Do you have any affiliation with the
23 University of Washington, past or present?

24 A. No, I do not have any affiliation with
25 the University of Washington either in the past or

1 at the moment.

2 Q. And I should say of course other than
3 this case.

4 A. That's correct, other than this case.

5 Q. Are you familiar with a company named
6 TwinStrand Biosciences?

7 A. Yes, I am familiar with TwinStrand.

8 Q. How are you familiar with TwinStrand?

9 A. I understand that TwinStrand is a
10 biotechnology company that sells a product that is
11 related to duplex sequencing.

12 Q. And the patent that's subject to this
13 proceeding is the '127 patent; correct? I'll give
14 you the whole number. 10,760,127 patent; is that
15 correct?

16 A. That's correct. I understand this
17 proceeding involves the patent 10,760,127, which
18 is currently assigned to UW.

19 Q. Is the '127 patent licensed to
20 TwinStrand?

21 A. So -- I'm not aware of any specific
22 licenses of the '127 patent, so I wouldn't want to
23 answer with absolute certainty.

24 Q. But you're aware that TwinStrand has an
25 interest in the '127 patent; correct?

1 A. Yes, that's correct.

2 Q. Do you have any financial interest in
3 TwinStrand?

4 A. No, I have no financial interest in
5 TwinStrand.

6 Q. Other than being a witness in this
7 case, do you have any affiliation with TwinStrand?

8 A. No, I have no affiliation with
9 TwinStrand.

10 Q. Are you a witness in any other cases
11 for TwinStrand?

12 A. Can you define what you mean by any --
13 this specific case?

14 Q. Other than this case, are you a witness
15 in any other cases for TwinStrand?

16 A. So I believe there may be multiple
17 proceedings involving different patents, and
18 there's a possibility that I may be a witness in
19 other IPRs as well.

20 Q. But you haven't appeared as a witness
21 in any other IPRs for TwinStrand; is that correct?

22 A. Correct, I have not appeared as a
23 witness in any other IPRs for TwinStrand.

24 Q. Have you appeared as a witness for any
25 other cases for the University of Washington?

1 A. No, I have not appeared as a witness in
2 any other case for the University of Washington.

3 Q. Other than this IPR have you ever
4 served as a consultant for TwinStrand?

5 A. Yes, I have served as a consultant for
6 TwinStrand outside of this IPR.

7 Q. In what capacity were you a consultant?

8 ATTORNEY POWERS: Objection to the
9 extent that calls for privileged information.
10 I'll instruct the witness not to answer.

11 Q. You can answer with the exception of
12 divulging privileged information.

13 ATTORNEY POWERS: I'll instruct the
14 witness not to answer.

15 Q. The question is still pending. Have
16 you worked as a consultant for TwinStrand?

17 ATTORNEY POWERS: I'll instruct the
18 witness not to answer on the grounds of
19 privilege.

20 ATTORNEY ROSATO: I'm not asking for
21 privileged information; I'm just asking if
22 he's worked as a consultant.

23 ATTORNEY POWERS: You can answer yes or
24 no.

25 A. Yes.

1 Q. When was that?

2 A. I can't give you an exact date, but I
3 believe it was about -- started about a year and a
4 half ago.

5 Q. About a year and a half ago would have
6 been the beginning of 2022; correct?

7 A. Yes, I believe that's correct.

8 Q. How did you come about being retained
9 as a witness in this proceeding?

10 A. So I received an email. I can't
11 remember exactly who the email was from.

12 ATTORNEY POWERS: And I'll just caution
13 the witness not to divulge communications with
14 counsel.

15 THE WITNESS: Okay.

16 Yes, but that's how I became first is
17 counsel reached out to me.

18 Q. That's counsel for Sterne Kessler?

19 A. Yes, that's correct.

20 Q. Counsel from Sterne Kessler.

21 A. That's right. Thank you.

22 Q. When did you start working on this
23 case?

24 A. I apologize, I can't remember the exact
25 date that I started.

1 Q. Was it before January of 2023?

2 A. Yes, it was before January of 2023.

3 Q. Was it before December of 2023?

4 A. Yes, it was before December of 2023.

5 Q. Before November?

6 A. Yes, it was before November of 2023.

7 Q. Do you think it dated back to October
8 2022?

9 A. I apologize, but I can't give an exact
10 date.

11 Q. Prior to this case have you ever served
12 as a witness in a legal proceeding?

13 A. Yes, I have.

14 Q. What cases?

15 A. So I have been a witness in couple of
16 cases. I'm just trying to remember -- am I
17 allowed to divulge that information?

18 Q. You're asking me. You should ask
19 counsel sitting here. But my answer to that would
20 be if it's publicly known that's what I'm asking
21 about.

22 A. Okay.

23 ATTORNEY POWERS: Do you understand the
24 question?

25 THE WITNESS: I do.

1 I'm not certain which cases are
2 public -- I'll answer for the ones that I'm
3 certain are publicly known. Is that all
4 right?

5 Q. Uh-huh.

6 A. So I had previously served as an expert
7 witness in a patent litigation between 10x
8 Genomics and Celsee, and I believe that's the only
9 case where I can be confident that the proceedings
10 were publicly known.

11 Q. What's the nature of that case, 10x
12 Genomics versus Celsee?

13 ATTORNEY ROSATO: That's, for the court
14 reporter, C-E-L-S-E-E.

15 A. So 10x Genomics and Celsee are both
16 biotechnology companies that sell products related
17 to single-cell sequencing analysis. And 10x had
18 initiated a lawsuit against Celsee on the grounds
19 that Celsee had infringed on some of its patents,
20 and so I was retained on behalf of Celsee in that
21 matter.

22 Q. So patent infringement case, is your
23 understanding?

24 A. I believe there were multiple issues,
25 as there often are: advertising issues,

1 employment issues. But the specific areas that I
2 was involved in were related to patent
3 infringement, amongst other things.

4 Q. And I think you said you were a witness
5 for Celsee; is that correct?

6 A. That's correct. At some point Celsee
7 was bought by a company named Bio-Rad, so I don't
8 know officially who -- how that affected the
9 precise nature of the litigation. But I was
10 originally retained by Celsee.

11 Q. And were you an expert witness in your
12 witness capacity?

13 A. Yeah, that's correct, I was an expert
14 witness.

15 Q. And you were a witness adverse to 10x
16 Genomics; is that correct?

17 A. Yes, that's correct.

18 Q. Are you familiar with a case where 10x
19 Genomics is adverse to NanoString Technologies?

20 A. Yes, I am familiar with that case.

21 Q. Are you a witness in that case?

22 A. I'm not certain if I can publicly
23 divulge that information.

24 Q. You don't know if you can publicly
25 divulge you're a witness on behalf of 10x

1 Genomics?

2 A. I have not previously appeared as a
3 witness in any legal proceedings on behalf of 10x
4 Genomics.

5 Q. You were adverse to 10x Genomics in the
6 Celsee case; correct?

7 A. Yes, that's correct.

8 Q. And currently 10x Genomics is adverse
9 to NanoString -- is that correct? -- in a
10 different case?

11 A. A different case, but I believe that is
12 correct.

13 Q. Are you familiar with the company
14 NanoString?

15 A. Yes, I am.

16 Q. How are you familiar with them?

17 ATTORNEY POWERS: Objection, relevance.
18 You can answer.

19 A. I was previously a member of the
20 scientific -- of a scientific advisory board for
21 NanoString.

22 Q. When did you join as a member of the
23 scientific advisory board for NanoString?

24 A. It was a while ago. I apologize that I
25 can't give an exact date.

1 Q. When did you terminate your position as
2 member of NanoString's scientific advisory board?

3 A. I apologize, I couldn't give an exact
4 date for when I terminated my position. But as
5 your question implies, I am no longer a member of
6 the scientific advisory board.

7 Q. Did your departure occur after you
8 signed on to be an expert for 10x Genomics in that
9 case?

10 A. I can't -- I can't remember the exact
11 order of events in that case.

12 Q. Are you aware you're subject to an
13 action to disqualify you as a witness in that
14 case?

15 A. I'm aware that there was a proceeding;
16 although I'm also aware of the outcome of that
17 proceeding, and I was not disqualified.

18 Q. So you're aware this is publicly
19 available information?

20 A. I don't know exactly what's publicly
21 available and what's not, and I'm not an attorney.
22 I apologize. I know there are databases where
23 presumably some of the documents from that action
24 might be available, but I don't know.

25 Q. Let's get you a copy of your

1 declaration. Actually, it looks like you have a
2 copy in front of you; is that correct?

3 A. That's correct.

4 Q. And just to be sure we're looking at
5 the same declaration, this is Exhibit 2014 in this
6 proceeding; is that correct?

7 A. Yes, I see that on the front page,
8 University of Washington EX 2014.

9 ATTORNEY ROSATO: Counsel, do you need
10 a copy?

11 ATTORNEY POWERS: I would love one.
12 Thank you.

13 Q. Dr. Satija, you have a copy of your
14 declaration; is that correct?

15 A. That's correct.

16 Q. And that's a copy that you brought with
17 you today; is that correct?

18 A. Yes, that's correct.

19 Q. Are there any notes in that copy that
20 you brought with you?

21 A. No, this is an unmarked fresh copy of
22 my declaration.

23 Q. In paragraph 7 of your declaration you
24 indicate you have a graduate degree in statistics;
25 is that correct?

1 A. Yes, that's correct. As I say in my
2 declaration, I received my DPhil in statistics at
3 the University of Oxford in 2010. I attended
4 Oxford University on a Rhodes scholarship.

5 Q. In paragraph 8 you mention working with
6 technologies that involve DNA sequencing; is that
7 correct?

8 A. Yes, that's correct.

9 Q. What DNA sequencing platforms have you
10 worked with?

11 A. So I've been working in DNA sequencing
12 and doing -- performing research on technologies
13 that involve DNA sequencing for pretty much my
14 entire career. So I've worked with a wide variety
15 of platforms, including Illumina sequencing,
16 PacBio sequencing, Oxford nanopore sequencing,
17 Sanger sequencing, SOLiD sequencing. And I don't
18 think that's a full list, but that's an example of
19 some of the types of technologies that I've worked
20 with over my career.

21 Q. What experience do you have working
22 with the Illumina sequencing platform?

23 A. So my laboratory at the New York Genome
24 Center, also jointly affiliated with New York
25 University, develops tools and technologies that

1 often utilize DNA sequencing approaches. We have
2 a particular interest in profiling nucleic acids
3 that are present in small samples, including
4 single cells. And so we use a variety of DNA
5 sequencing technologies, including Illumina, to
6 profile those nucleic acids.

7 Q. You mentioned New York University;
8 correct?

9 A. That's correct. I'm an associate
10 professor with tenure at New York University.

11 Q. New York University does not have a
12 PacBio sequencing machine; is that correct?

13 A. I couldn't say with certainty what
14 instrumentation. It's a large university. So I
15 couldn't say that with certainty.

16 Q. Do you have any knowledge of a Pacific
17 Biosciences platform at NYU?

18 A. So there are probably hundreds of
19 biological labs in core facilities at NYU. So
20 while I don't at the moment know of a specific
21 PacBio machine, it's entire possible that one
22 exists at NYU.

23 Q. But you personally have not worked with
24 a PacBio machine at NYU; correct?

25 A. At New York University I have not

1 personally worked with -- on site at New York
2 University I have not worked with a PacBio
3 sequencing machine. But, again, it's entirely
4 possible that one does exist there.

5 Q. Page 29 of your declaration you have a
6 section that is titled the '127 patent claims. Do
7 you see that?

8 A. Yes, I see that section.

9 Q. The next page, page 30, the section
10 begins, the meaning of claim terms, claim
11 construction. Do you see that?

12 A. Yes, I see that.

13 Q. And that section spans paragraphs 50
14 through 65. Did I get that correct?

15 A. Yes, that's correct.

16 Q. And you discuss two terms in that
17 section of the declaration; is that correct?

18 A. Not exactly, no.

19 Q. Well, there's two subheadings; is that
20 correct?

21 A. That's correct, but there's a
22 subheading A and a subheading B.

23 Q. Is there a subheading C?

24 A. No. There is a subheading A and a
25 subheading B.

1 Q. Subheading A recites, amplifying
2 adapter DNA molecules to produce strand copies; is
3 that correct?

4 A. That's correct.

5 Q. And subheading B recites, first and
6 second strand sequencing reads; is that correct?

7 A. Yes, that's correct.

8 Q. And as you indicated, there are no
9 other subsections here; correct?

10 A. There is no subheading C. And as
11 you -- and this section in my report spans
12 paragraphs 50 to 65.

13 Q. At paragraph 60 you state, A POSA
14 reading this claim would understand that a
15 sequence read refers to a contiguous set of DNA
16 nucleotides that correspond to the output of a DNA
17 sequencing reaction such as the sequencing by
18 synthesis process depicted in Figure 1.

19 Do you see that?

20 A. Yes, I see that.

21 Q. And for terminology purposes, a POSA is
22 a person of ordinary skill in the art; is that
23 correct?

24 A. Yes, that is correct.

25 Q. In that sentence you refer to "this

1 claim." Do you mean Claim 1?

2 A. So, as I say in my declaration in this
3 action, Claim 1 does recite sequencing a plurality
4 of first and second strand copies to obtain first
5 and second strand sequence reads.

6 I also point out that Claims 2 through
7 21 depend from Claim 1 and thus also include this
8 limitation.

9 Q. My question is when you say "this
10 claim" what claim are you referring to.

11 A. Just so that I can be certain, would it
12 be possible for me to see a copy of the '127
13 patent?

14 Q. Sure. I am handing you a copy of the
15 '127 patent which has obviously been filed, and
16 it's marked as Exhibit 1001 in this proceeding.

17 (Pause.)

18 A. All right. So in this section of my
19 declaration, I give my opinion that a person of
20 ordinary skill in the art would understand that a
21 sequence read refers to a contiguous set of DNA
22 nucleotides that correspond to the output of a DNA
23 sequencing reaction.

24 And I go further to state that a person
25 of ordinary skill in the art would understand

1 first and second strand sequence reads to mean
2 distinct sequence reads of the first strand and a
3 second distinct sequence read of the second
4 strand.

5 Those specific terms of course appear
6 in the claims. So in that paragraph I use the
7 words "this claim," but I want to highlight that
8 multiple claims in the specification involve these
9 terms.

10 Certainly Claim 1 utilizes the terms
11 first and second strand sequence reads, but also
12 Claim 3 uses these terms. For example, Claim 3
13 uses the language comparing the confirmed first
14 strand sequence read and confirmed second strand
15 sequence read.

16 And as I say in my declaration, Claims
17 2 through 21 depend from Claim 1, of course, and
18 also include this terminology.

19 So my statement in paragraph 60 is not
20 meant to only be applied to Claim 1 but, as I say,
21 covers the way that a person of ordinary skill in
22 the art would interpret these terms throughout the
23 claims.

24 Q. And your statement here is saying that
25 a POSA reading this claim would come to that

1 understanding; is that correct?

2 A. So the specific words that I list in
3 that sentence are a POSA reading this claim. But
4 in the broader context of the paragraph, I am very
5 clear that my opinion applies to the use of these
6 terms which occur in multiple claims throughout
7 the specification.

8 Q. You're saying this is a mistake to say
9 "this claim"?

10 A. I don't believe I said that it was a
11 mistake.

12 Q. Okay. Then my question is what claim
13 specifically are you referring to when you make
14 that statement.

15 A. So the statement that I make -- and in
16 this paragraph, as I said, I provide an opinion on
17 how a person of ordinary skill in the art would
18 interpret the term sequence read and in particular
19 how a person of ordinary skill in the art would
20 interpret a first and second strand read to mean
21 distinct sequencing reads corresponding two
22 separate DNA sequencing reactions. That's the
23 opinion that I offer.

24 You're asking me the context in which
25 I'm offering that opinion. Certainly that opinion

1 applies to Claim 1, but, as I say in this
2 paragraph, it also applies to additional claims
3 that depend on Claim 1 and include this
4 limitation.

5 Q. You're not answering my question. If
6 you continue to do that, we're going to be here a
7 really long time. Do you understand that?

8 A. I do.

9 Q. Some of these questions I'll ask you
10 are not trick questions. Do you understand that?

11 A. I do. But it's also important that I
12 speak accurately and truthfully, as I'm under
13 oath.

14 Q. I agree. And how you spoke in your
15 declaration is used the singular term "this
16 claim"; correct?

17 A. The words on the page that I state are
18 "this claim," but at no point in my declaration do
19 I say that my interpretation or my opinion is
20 limited to a single claim.

21 Q. Nor has anyone suggested that. The
22 question pending to you is what claim are you
23 referring to when you say "this claim."

24 ATTORNEY POWERS: Objection, asked and
25 answered.

1 A. I apologize that I'll give a similar
2 answer as before. In this paragraph I offer an
3 opinion on how a person of ordinary skill in the
4 art would interpret the terms first and second
5 strand sequence reads.

6 Those terms appear in Claim 1, which is
7 the beginning of paragraph 60, but I also say that
8 Claims 2 through 21 depend from Claim 1 and thus
9 also include this limitation.

10 Q. Earlier you indicated you're not
11 seeking to modify your testimony as stated here in
12 the declaration; is that correct?

13 A. I am not seeking to modify my
14 testimony.

15 Q. You also mention the sequencing by
16 synthesis process depicted in Figure 1 -- is that
17 correct? -- referring to paragraph 60?

18 A. Yes, I do say that in my declaration.

19 Q. Are you interpreting the claims of the
20 '127 patent as limited to the process depicted in
21 Figure 1?

22 A. I don't believe that's what I say in my
23 declaration.

24 Q. Sitting here today are you interpreting
25 the claims of the '127 patent as limited to the

1 process depicted in Figure 1 of the '127 patent?

2 (Pause.)

3 A. Sorry, could you repeat the question?
4 I was just reading the description of Figure 1.

5 Q. Sitting here today are you interpreting
6 the claims of the '127 patent as limited to the
7 process depicted in Figure 1 of the '127 patent?

8 ATTORNEY POWERS: Objection, scope.

9 A. So when I cite Figure 1 in my
10 declaration, I say that a person of ordinary skill
11 in the art reading this claim would understand
12 that a sequence read refers to a contiguous set of
13 DNA nucleotides that correspond to the output of a
14 DNA sequencing reaction such as the sequencing by
15 synthesis process depicted in Figure 1.

16 So I'm giving an example of a type of
17 sequencing reaction that would be relevant to this
18 set of claims.

19 The description of Figure 1 in the '127
20 patent specification is an overview of the duplex
21 consensus sequencing process.

22 So these are overview figures and
23 examples. They are not meant to be a restrictive
24 set of limitations, as your question suggests.

25 Q. So you indicated Figure 1 as an

1 example; is that correct?

2 A. That's not correct. That's not --
3 that's not the specific words that I said.

4 Q. Did you describe Figure 1 as an
5 example?

6 A. I did not. I described the sequencing
7 by synthesis process depicted in Figure 1 as an
8 example of a DNA sequencing reaction.

9 Q. And is your opinion that the claims of
10 the '127 patent are limited to that example
11 illustrated in Figure 1?

12 ATTORNEY POWERS: Objection, asked and
13 answered.

14 A. So Figure 1 is an overview of a duplex
15 consensus sequencing method. It is a schematic
16 figure. It is not a precise set of limitations by
17 which to interpret the claims.

18 Q. Thank you.

19 What is your understanding of what
20 process is depicted in Figure 1?

21 A. So Figure 1 -- I'm referring now to the
22 legend in the '127 patent specification which is
23 on Column 3. It illustrates an overview of the
24 duplex consensus sequencing process, and it
25 describes a series of steps, including the

1 sheering of double-stranded DNA, the ligation of
2 specific types of adapters, the PCR amplification
3 with a specific type of flow cell compatible tail,
4 and further downstream processing steps.

5 Q. Does Figure 1 depict adapter molecules?
6 (Pause.)

7 A. So in Figure 1 there is a -- about
8 halfway down the figure there is an annotation:
9 PCR with flow cell adapter sequence.

10 Q. Are you indicating that's where adapter
11 molecules are depicted?

12 A. That is one example of the use of the
13 word "adapter" in Figure 1.

14 Q. Do you see adapter molecules depicted
15 in the figure in illustrative terms?

16 A. Yes.

17 Q. Where do you see them?

18 A. So there are different types of adapter
19 and molecules that are included in this figure.
20 In that specific example that I mentioned earlier
21 for adapter sequence, I believe that those
22 adapters are schematicized in the lines that are
23 located next to that annotation.

24 Q. You're referring to the annotation in
25 the middle of the figure as you move top to

1 bottom; is that correct?

2 A. That's one example.

3 Q. Is another example the schematic at the
4 top of the figure?

5 A. Is that an example of -- sorry, what --
6 can you repeat the question?

7 Q. Where else are adapter molecules
8 depicted in the figure?

9 A. So in the top schematic on the figure
10 also depicts Y-shaped adapter molecules.

11 Q. And in that top figure which of the --
12 well, let me -- strike that.

13 The top figure shows three different
14 objects; is that correct?

15 (Pause.)

16 A. There are three -- there are multiple
17 components to that figure. The word "object"
18 isn't precisely defined, but I think I understand
19 what you're saying.

20 Q. Is the component in the middle an
21 adapter?

22 A. The component in the middle is titled
23 T-tailed DNA fragment. Is that the component that
24 you're referring to?

25 Q. Yes.

1 A. No, that is not an adapter molecule.

2 Q. And the adapter molecules are the
3 components on the left and right of that T-tailed
4 DNA fragment; is that correct?

5 A. So as the legend of Figure 1 describes,
6 the middle component -- this is one embodiment of
7 the invention, but the middle component
8 corresponds to sheared double-stranded DNA that
9 has been end repaired and T-tailed.

10 Actually, I've forgotten your question.
11 I apologize.

12 Q. We're trying to find the adapters.
13 Which ones are they?

14 A. The A-tailed -- sorry, the A-tailed SMI
15 adapters are the Y-shaped components.

16 Q. And those are the components on the
17 left and right of the DNA fragment depicted at the
18 top of Figure 1; correct?

19 A. Yes, that's correct.

20 Q. Earlier you mentioned Y-shaped
21 adapters; correct?

22 A. Yes, I used the term "Y-shaped
23 adapters."

24 Q. Are these Y-shaped adapters at the top
25 of Figure 1?

1 A. Yes, these are examples of Y-shaped
2 adapters.

3 Q. And were Y-shaped adapters known in the
4 prior art prior to the '127 patent?

5 A. Yes, I believe that's correct.

6 Q. Figure 1 mentions the term "ligation."
7 Do you see that?

8 A. Yes, I see that word.

9 Q. What is being ligated?

10 ATTORNEY POWERS: Object to form.

11 A. So, again, just to be precise, I will
12 refer to the legend for Figure 1 in the '127
13 specification, which states that the sheared
14 double-stranded DNA is ligated and combined -- is
15 combined with the A-tailed SMI adapters.

16 Q. Can you turn to Example 3 of Column 25,
17 please? Let me know when you're there.

18 A. Could I have a minute to read it,
19 please?

20 Q. Yes.

21 (Pause.)

22 A. Okay. Thank you.

23 Q. The bottom of Column 25 discusses
24 ligation of Illumina TruSeq DNA sequencing
25 adapters. Do you see that?

1 A. I do see that.

2 Q. What are Illumina TruSeq DNA sequencing
3 adapters?

4 A. So Illumina is a biotechnology company
5 that offers a number of products, including
6 technologies for massively parallel and next-
7 generation DNA sequencing. They also sell DNA
8 oligonucleotide adapter molecules, including the
9 Illumina TruSeq DNA sequencing adapters, that can
10 be used to facilitate the analysis of DNA
11 oligonucleotides with Illumina sequencing
12 technology.

13 Q. Are Illumina TruSeq DNA sequencing
14 adapters Y-shaped adapters?

15 A. I believe so, yes.

16 Q. And are Illumina TruSeq DNA sequencing
17 adapters considered palindromic adapters?

18 ATTORNEY POWERS: Objection,
19 foundation.

20 A. I do know that Illumina TruSeq is a --
21 it's a product name, but it's not a specific
22 version of the product. So there could be, for
23 example, multiple different sequences that
24 correspond that all have the name Illumina TruSeq
25 adapters.

1 For example, the Illumina sequencing
2 technology has changed over time. And as new
3 Illumina machines are created, the specific
4 sequence of the TruSeq DNA sequencing adapter will
5 also change.

6 So I couldn't answer with certainty
7 whether this -- all Illumina TruSeq DNA sequencing
8 adapters would be considered palindromic.

9 Q. Would you expect that the Illumina
10 TruSeq DNA sequencing adapters used here in
11 Example 3 are palindromic?

12 A. So I wouldn't want to speculate
13 specifically on exactly what Illumina TruSeq
14 adapters were being used here.

15 Q. So you don't know what adapters were
16 being used here; is that accurate?

17 A. I don't believe that's accurate.

18 Q. Do you know what Illumina TruSeq
19 sequencing adapters are being used here?

20 ATTORNEY POWERS: Object to form.

21 A. So I do know that Illumina TruSeq DNA
22 sequencing adapters are being used based on what's
23 written in the specification. I do not know the
24 exact sequence of those Illumina TruSeq DNA
25 sequencing adapters because that name of a product

1 can refer to multiple different types of sequences
2 over time.

3 Q. Based on what you see here in Example
4 3, do you have enough information to say whether
5 these Illumina TruSeq DNA sequencing adapters used
6 in Example 3 are palindromic?

7 ATTORNEY POWERS: Objection, form,
8 foundation.

9 A. Again, I'm under oath. I want to be
10 able to speak accurately and specifically. And I
11 wouldn't want to answer that question with a
12 specific yes or no answer without being aware of
13 the exact oligonucleotide sequence of the Illumina
14 TruSeq DNA sequencing adapter, which can change
15 over time.

16 Q. Does Example 3 provide a sequence of
17 these Illumina TruSeq DNA sequencing adapters?

18 (Pause.)

19 A. So in the '127 patent specification the
20 section discussing Example 3 spans Columns 25, 26,
21 and 27. And nowhere in those columns do I see a
22 full enumeration of the oligonucleotide sequence
23 that corresponds to the Illumina TruSeq DNA
24 sequencing adapters.

25 Q. That same sentence at the bottom of

1 Column 25 that we're looking at -- let me know
2 when your attention is back there.

3 A. Okay.

4 Q. That sentence refers to standard
5 library preparation methods. Do you see that?

6 A. I do see that.

7 Q. What are standard library preparation
8 methods?

9 A. So I don't believe this language is
10 particularly precise, but I do have experience
11 with the generation of DNA sequencing libraries.
12 And reading that particular sentence or those
13 words in context, I believe that the authors are
14 referring to a series of steps that are commonly
15 performed in the generation of DNA sequencing
16 libraries. Those steps include end repair,
17 A-tailing, and ligation. And I believe that is
18 what the inventors are -- or the authors are
19 referring to here.

20 Q. You mentioned your experience; is that
21 correct?

22 A. That's correct.

23 Q. And did you bring your experience to
24 bear in interpreting that sentence in the '127
25 patent specification?

1 A. Throughout this case the opinions that
2 I offer, certainly I used my scientific experience
3 and expertise in offering my opinions.

4 Q. In the course of reading this patent
5 and interpreting it, were you bringing to bear
6 your experience as a person of ordinary skill?

7 A. Yes, I was.

8 Q. So as a person of ordinary skill
9 reading this sentence, you have some understanding
10 of what standard library preparation methods
11 constitute; is that correct?

12 ATTORNEY POWERS: Object to form,
13 foundation.

14 A. Can you just repeat the question?

15 Q. Yeah. As a person of ordinary skill
16 reading this sentence, you have some understanding
17 of what standard library preparation methods
18 constitute; is that correct?

19 ATTORNEY POWERS: Objection, form,
20 foundation.

21 A. Yes, that's correct.

22 Q. And that's true even though this
23 example does not list out those standard library
24 preparation methods; is that accurate?

25 A. Yes, that's correct. As a person of

1 ordinary skill in the art, either myself or a
2 hypothetical person of ordinary skill in the art
3 would understand this sentence.

4 Q. Should the patent have listed those
5 methods specifically?

6 ATTORNEY POWERS: Object to form.

7 A. I'm actually going to slightly modify
8 something I said before, which is that the
9 language here was -- I don't remember exactly the
10 words that I used. I believe a person of ordinary
11 skill in the art would understand this sentence.

12 ATTORNEY POWERS: Mike, we've been
13 going about an hour. Is now a good time to
14 take a break?

15 ATTORNEY ROSATO: Let's take a few
16 minutes and we'll take a break.

17 THE WITNESS: I'd like to take a break,
18 if that's okay.

19 ATTORNEY ROSATO: Yeah, let's just get
20 through a couple of questions. We'll be at a
21 good break time.

22 ATTORNEY POWERS: Two minutes?

23 ATTORNEY ROSATO: Yeah, about that.

24 ATTORNEY POWERS: Is that okay.

25 THE WITNESS: That's okay.

1 Q. Is it fair to say that if reaction
2 conditions or methods are standard or known in the
3 art it's not necessary to list them out in this
4 patent here?

5 ATTORNEY POWERS: Objection, legal
6 conclusion.

7 A. So I think you're asking a very broad
8 question about generally what's necessary to list
9 in patents and what's not. In this case I don't
10 believe it was necessary. But I would -- I don't
11 want to answer generally for all patents in all
12 cases.

13 Q. And part of the reason you don't think
14 it's necessary is because you brought your
15 experience as a person of ordinary skill to bear
16 in interpreting this; is that accurate?

17 ATTORNEY POWERS: Object to form,
18 foundation.

19 A. So certainly when reading this sentence
20 I can read it through the lens of a person of
21 ordinary skill in the art in 2012. And standard
22 library preparation methods were well known in the
23 art as of March 2012.

24 Q. Turning to page 11 of your declaration,
25 you list Exhibit 1012. Do you see that?

1 A. Yes, I do see that.

2 Q. I'll hand you a copy of Exhibit 1012.

3 Do you recognize this document?

4 A. Can I have a minute to read it?

5 Q. Sure.

6 (Pause.)

7 A. Thank you. I do recognize this
8 document as an exhibit that I relied upon in my
9 report.

10 Q. And what is Exhibit 1012?

11 A. So it's a document in front of me. It
12 was prepared, it appears, by Illumina. On the
13 header it's titled data sheet Illumina sequencing.
14 And data sheets are often pieces of information
15 that Illumina will make available to customers as
16 an introduction to some of their products. They
17 are not detailed experimental protocols, but they
18 represent sort of an overview of what the product
19 is and how it can be used.

20 Q. Page 11 of your declaration you
21 identify Exhibit 1012 as Illumina TruSeq RNA and
22 DNA sample preparation kits data sheet Illumina
23 sequencing 2010; is that correct?

24 A. Yes, that's what's written in my table
25 on page 11 of my report.

1 Q. Great.

2 ATTORNEY POWERS: Time for a break?

3 ATTORNEY ROSATO: Yes.

4 (Recess taken from 10:07 to 10:19.)

5 Q. Let's turn back to Figure 1 of the '127
6 patent, and let me know when you're there, please.

7 A. Okay. I'm here.

8 Q. Figure 1 mentions size selection. Do
9 you see that?

10 A. I do see that, yes.

11 Q. Is something being selected based on
12 size?

13 ATTORNEY POWERS: Object to form.

14 (Pause.)

15 A. Maybe you could clarify what you mean
16 by "something."

17 Q. What is size selection referring to?

18 A. So, for example, going back to the
19 specification, which was a legend for Figure 1 in
20 Column 3, the legend states, after size selecting
21 for appropriate length fragments. I believe
22 that's what the figure is referring to in the
23 context of size selection.

24 Q. By "fragments" is it referring to DNA
25 fragments?

1 A. I believe so, yes.

2 Q. In 2012 were any DNA fragment size
3 selection methods known in the art?

4 A. Yes, there were size selection methods
5 that were known in the art.

6 Q. What DNA fragment size selection
7 methods would have been known to a person of
8 ordinary skill at the time?

9 A. So there are different methods for size
10 selection. Many of them have advantages and
11 disadvantages. Some size selection methods are
12 tailored towards particular size ranges. Other
13 size selection methods can result in a substantial
14 loss of material.

15 So there are a variety of methods, but
16 they do have advantages and disadvantages.

17 Q. Would those advantages and
18 disadvantages have been known to a person of
19 ordinary skill at the time?

20 A. I believe so, yes.

21 Q. Are you familiar with gel
22 electrophoresis?

23 A. I am, yes.

24 Q. What is gel electrophoresis?

25 A. So gel electrophoresis is a method of

1 analyzing a collection of DNA oligonucleotides
2 where the DNA oligonucleotides are exposed to an
3 electric current and the electric current causes
4 DNA oligonucleotides to move through a gel-like
5 material.

6 Q. As of 2012 was gel electrophoresis used
7 to distinguish DNA fragments based on size?

8 A. It would be helpful if you could give
9 some context on the word "distinguish."

10 Q. As of 2012 was gel electrophoresis used
11 as a method to separate DNA fragments based on
12 size?

13 A. So gel electrophoresis on its own is
14 not a method for size selection, for example.

15 Q. As of 2012 was it used for size
16 selection of DNA fragments?

17 ATTORNEY POWERS: Object to form.

18 A. As of 2012 there were methods for size
19 selection that utilized a gel electrophoresis
20 step, but these methods did have disadvantages.

21 Q. Was it a known method at the time?

22 ATTORNEY POWERS: Objection, asked and
23 answered.

24 A. So gel electrophoresis -- there were a
25 variety -- as I've said before, there were a

1 variety of size selection methods that were known
2 in the art as of 2012, each of which has
3 advantages and disadvantages.

4 There were methods for size selection
5 that utilized a gel electrophoresis step, but
6 these methods did have disadvantages that would
7 have been known to a person of ordinary skill in
8 the art.

9 Q. Would a person of ordinary skill in the
10 art knowing advantages and disadvantages bring
11 that information to bear in selecting a particular
12 size selection method used in a given experiment?

13 ATTORNEY POWERS: Object to form.

14 A. I believe that when pursuing any
15 scientific experiment a person of ordinary skill
16 in the art would be able to utilize their
17 expertise and knowledge of advantages and
18 disadvantages of a method that were known in the
19 art.

20 Q. Do you recall what size selection
21 methods are discussed in the '127 patent?

22 (Pause.)

23 A. So I don't recall a comprehensive list.
24 I do know that DNA size selection methods are
25 discussed. I'm happy to read through the entire

1 patent, if you'd like, to make sure -- to refresh
2 my memory, but I'm happy to -- I do know that size
3 selection methods were discussed.

4 Q. Why don't we turn to Example 1 at
5 Columns 19 through 20 of the '127 patent. Let me
6 know when you're there.

7 A. I'll read it briefly, if that's okay.
8 (Pause.)

9 A. Okay. Thank you.

10 Q. Bottom of Column 19 states, DNA
11 fragments larger than the optimal range of about
12 200 to 500 base pairs were removed by adding .7
13 volumes of AMPure XP beads.

14 Do you see that?

15 A. I do see that.

16 Q. What are AMPure beads?

17 A. So AMPure beads are a molecular biology
18 reagent. I believe they are manufactured and sold
19 by a company called Agencourt. This is a reagent
20 we use quite frequently in my research lab, so we
21 are familiar with the advantages and disadvantages
22 of this method. But the -- well, that's the
23 answer to your question.

24 Q. Thank you.

25 Are the AMPure beads being used here in

1 Example 1 for DNA fragment size selection?

2 A. AMPure beads in this example are --
3 I'll just read from the specification. They are
4 used to remove DNA fragments that are larger than
5 200 to 500 bases.

6 Q. Thereby leaving DNA fragments in the
7 200 to 500 base pair range; is that correct?

8 A. So I should highlight that, as with
9 many molecular biology reagents, the AMPure bead
10 selection process is not perfect. So there will
11 be a potentially significant portion -- well,
12 there can be DNA molecules that are larger than
13 200 to 500 bases. But certainly the goal of the
14 procedure is to enrich for DNA molecules of a
15 particular -- in this case 200 to 500 bases pair
16 size.

17 Q. And you indicated that AMPure beads
18 were commercially available in 2012; is that
19 correct?

20 A. I believe that's correct, yes.

21 Q. I could of course break that down. You
22 indicated AMPure beads were commercially
23 available; is that correct?

24 A. Since this was 12 years ago, I can't
25 say with certainty that they didn't receive this

1 through some noncommercial means. But certainly
2 the language of the specification indicates that
3 they purchased this reagent from Agencourt.

4 Q. Do you see at Column 12 lines 5 through
5 6 -- excuse me. Do you see at Column 20, lines 5
6 through 6, where the patent states the beads were
7 washed and DNA eluted?

8 A. I do see that step, yes.

9 Q. And just to be clear, that's at Column
10 20, lines 5 through 6 of the '127 patent; correct?

11 A. Yes, that's correct.

12 Q. Does it state here what the beads were
13 washed with?

14 A. In this statement a specific wash
15 buffer is not named.

16 Q. Does it matter what buffer the beads
17 were washed with?

18 ATTORNEY POWERS: Object to form.

19 A. While it does matter what the beads --
20 what buffer the beads were washed in, there are a
21 variety of buffers that are compatible with the
22 wash step when using AMPure XP beads in an example
23 like this.

24 Q. And you used the term "buffer";
25 correct?

1 A. Yes, that's correct.

2 Q. The term "buffer" is not recited in the
3 sentence we read, is it?

4 A. The word "buffer" does not appear, but
5 a person of ordinary skill in the art would
6 understand that when performing a wash step that
7 would be referring to adding a reagent to a
8 sample. That reagent is commonly referred to as a
9 wash buffer. And then removing -- subsequently
10 removing that reagent.

11 Q. Are there wash buffers that would not
12 elicit DNA elution?

13 ATTORNEY POWERS: Object to form.

14 A. That is a very broad question about
15 whether any possible chemical would elicit DNA
16 elution, and I would disagree with that statement.

17 Q. Can you clarify what you're disagreeing
18 with?

19 A. The idea that any possible chemical
20 would elicit DNA elution.

21 Q. So you're saying not every chemical
22 would elicit DNA elution; is that correct?

23 A. Not every possible chemical will elicit
24 DNA elution. However, it was well known in the
25 art that there were a variety of buffers that

1 would have been compatible with DNA elution when
2 using AMPure XP beads for molecular steps like the
3 one recited here.

4 I'm happy to list some of those buffers
5 for you if you would like.

6 Q. It's fair to assume that they're using
7 a wash buffer that did in fact elicit DNA elution;
8 is that fair?

9 A. No, that's not fair at all.

10 Q. Is it fair to assume they used a wash
11 buffer that did not elicit DNA elution?

12 A. So traditionally when performing a wash
13 step, as is being performed here, the goal of that
14 wash step is to remove impurities from a sample
15 prior to facilitating DNA elution.

16 The language here, the beads were
17 washed and DNA eluted, a person of ordinary skill
18 in the art would understand that that corresponds
19 to two subsequent steps: a wash step to remove
20 impurities from a sample and then a DNA elution
21 step to elute specific DNA fragments from the
22 AMPure XP beads.

23 It is important to use a different
24 buffer for those two steps, which are often
25 referred to, for example, in the art as a wash

1 buffer or an elution buffer. And the reason it's
2 important to use different buffers is that if, for
3 example, the wash buffer were to facilitate DNA
4 elution, then the DNA would also be removed along
5 with the impurities from the sample.

6 So that's why it would be important and
7 was well known in the art to perform these wash
8 and elution steps separately and with different
9 buffers.

10 Q. That's helpful. Thank you.

11 So if I'm understanding correctly, this
12 is fairly interpreted as having separate washing
13 and elution steps; is that fair?

14 A. A person of ordinary skill in the art
15 would understand at this time that when performing
16 an AMPure XP reaction with the goal of obtaining
17 DNA fragments of a 200 to 500 base pair size that
18 there would be subsequent separate wash and
19 elution steps.

20 Q. And a person of ordinary skill would
21 understand that even though it's not stated here;
22 is that correct?

23 ATTORNEY POWERS: Object to form.

24 A. I believe it is stated here. The beads
25 were washed and DNA eluted.

1 Q. That could be interpreted to be a
2 single step; correct?

3 A. I don't believe that's correct.

4 Q. Well, the sentence we read doesn't
5 state that the beads were washed and eluted in two
6 separate steps.

7 ATTORNEY POWERS: Object to form.

8 A. So my understanding is a person of
9 ordinary skill in the art would read this sentence
10 in the broader context of the paragraph, the
11 specification as a whole, and of course what was
12 known in the art.

13 And a person of ordinary skill in the
14 art would understand that the beads were washed
15 and DNA eluted and that those would correspond to
16 subsequent -- or separate steps.

17 Q. Okay.

18 Does this example specify what buffer
19 was used for DNA elution?

20 (Pause.)

21 A. So -- there is a piece of information
22 in this paragraph that's very relevant to our
23 discussion, which I apologize I didn't see before.
24 Certainly consistent with all of my previous
25 answers, but I think it's important context.

1 So earlier in the paragraph the authors
2 state that DNA was purified with two volumes of
3 Agencourt AMPure XP beads per the manufacturer's
4 protocol. So the manufacturer's protocol,
5 certainly a person of ordinary skill in the art,
6 that would certainly list a specific wash buffer,
7 it would list a specific elution buffer, and it
8 would enumerate the fact that the wash step and
9 the elution step were performed in separate steps.

10 Q. Have you reviewed AMPure XP
11 manufacturer's protocol prior to this
12 conversation?

13 A. That is something that I am familiar
14 with generally in the expertise of using my -- in
15 my research laboratory.

16 Q. Do you recall specifically what's
17 stated in the manufacturer's protocol?

18 A. So I'm under oath, and I'd like to
19 speak with a hundred percent certainty to be
20 accurate.

21 So, for example, the manufacturer's
22 protocol does list potential wash buffers that can
23 be used. But sitting here today I can't tell you
24 the exact percentage of ethanol, as an example, of
25 what's present in those wash buffers.

1 But I do want to point out that the
2 authors do highlight that they performed this step
3 according to the manufacturer's protocol, and that
4 would have been relevant to a person of ordinary
5 skill in the art.

6 Q. Is it fair to say that if reaction
7 conditions or methods are already established or
8 known to a person of ordinary skill in the art
9 that they don't need to be listed out in the
10 patent?

11 ATTORNEY POWERS: Object to form.

12 A. Again, I think you're asking a very
13 broad question. When you say they don't need to
14 be, I'm not sure exactly what you're referring to
15 in the context of the word "need. " So I can't
16 answer that question generally.

17 Q. You seem to be understanding what might
18 be used or selected by a person of ordinary skill
19 in the art based on drawing from your experience
20 in the field; is that accurate?

21 A. Sorry, could you repeat the question?

22 Q. Would a person of ordinary skill draw
23 from their understanding of the art in
24 interpreting steps that might not be spelled out
25 specifically?

1 ATTORNEY POWERS: Objection to form.

2 A. So it's a very broad question, and I'm
3 not sure exactly what context a person would be
4 using this expertise for. But I do say in my
5 declaration that I understand a person of ordinary
6 skill in the art, a hypothetical person who is
7 presumed to be aware of all pertinent art, thinks
8 along conventional wisdom in the art, and is a
9 person of ordinary creativity.

10 Q. Where in your declaration are you
11 reading from?

12 A. I'm reading from paragraph 28.

13 Q. This is the sentence that reads, I
14 understand that a person of ordinary skill in the
15 art, POSA, is a hypothetical person who is
16 presumed to be aware of all pertinent art, thinks
17 along conventional wisdom in the art, and is a
18 person of ordinary creativity; is that correct?

19 A. That was the sentence I was referring
20 to, that's correct.

21 Q. Great. Thank you.

22 And that's not the only sentence here;
23 is that correct?

24 A. That is not the only sentence in my
25 declaration, that is correct.

1 Q. It's not the only sentence in Section 5
2 of your declaration that's titled person of
3 ordinary skill in the art; right?

4 A. That is also correct.

5 Q. Okay. Let's turn back to Figure 1 of
6 the '127 patent. Let me know when you're there.

7 A. Okay. I'm there.

8 Q. Does Figure 1 depict a barcode?

9 A. Yes.

10 Q. Where does Figure 1 depict a barcode?

11 A. To be precise, I'll go back to the
12 specification. So looking at the legend of Figure
13 1 in Column 3, the legend states that the adapter
14 molecules that we previously discussed contain
15 what's known as an SMI. And that SMI is an
16 acronym that's defined in the summary of the
17 invention also in the same column and refers -- is
18 referred to as a single-molecule identifier.

19 Q. Is the SMI a barcode?

20 (Pause.)

21 A. Yes, it is.

22 Q. You indicated that SMI stands for
23 single-molecule identifier; is that right?

24 A. That's correct.

25 Q. The term here is "identifier" not

1 "barcode"; is that correct?

2 A. The term is "SMI," which stands for
3 single-molecule identifier.

4 Q. And do you consider an identifier the
5 barcode?

6 A. Yes.

7 Q. Just so we're referring to the same
8 portions of Figure 1, the image at the top labels
9 SMI sequences. Do you see that?

10 A. I do see that.

11 Q. Is that what you consider barcode?

12 A. Yes.

13 Q. And by "sequences" is that nucleotide
14 sequences?

15 A. Which -- when you say "sequences," what
16 are you referring to?

17 Q. The term in Figure 1 is "SMI
18 sequences." My question is is that referring to
19 nucleotide sequences.

20 A. That's correct.

21 Q. What makes a nucleotide sequence a
22 barcode?

23 (Pause.)

24 A. So "barcode" is a term both that would
25 be familiar to a person of ordinary skill in the

1 art but is also used in the claims. Typically it
2 means that it is a nucleic acid sequence that's
3 used to label or to indicate a piece of
4 information, kind of in the same way that if you
5 go to the grocery store and you pick an item off
6 the shelf there is a barcode on there; and then
7 when you go to the cashier, the barcode sequence
8 indicates the specific item that you're trying to
9 purchase.

10 So it's important that that barcode
11 sequence provides some information. There are
12 different types of barcodes, but they will provide
13 some type of information.

14 Q. What type of information?

15 ATTORNEY POWERS: Object to form.

16 A. It would depend on the barcode and the
17 context in which it was being used.

18 Q. Information sufficient to identify
19 something?

20 A. That's certainly one possible use of a
21 barcode.

22 Q. And here in Figure 1 what you're
23 calling the barcode is in the adapter molecules;
24 is that correct?

25 A. Can you repeat the question, sorry?

1 Q. Here in Figure 1 what you're calling
2 the barcode is in the adapter molecules; is that
3 correct?

4 A. So in Figure 1 the depicted adapter
5 molecules comprise barcodes.

6 Q. And those barcodes are located in the
7 adapter molecule; is that correct?

8 A. The adapter molecules comprise
9 barcodes, is probably the most accurate way of
10 saying it.

11 Q. Do the adapter molecules comprise
12 "nucleotide sequences" that are not barcodes?

13 A. They can. It's a possibility.

14 Q. So here in Figure 1 do other portions
15 of the adapter illustrate a barcode?

16 ATTORNEY POWERS: Object to form.

17 A. Can you define what you mean by "other
18 portions of the adapter"?

19 Q. The adapters here I believe you
20 previously indicated are Y-shaped adapters; is
21 that correct?

22 A. That's correct.

23 Q. And those Y-shaped adapters have
24 noncomplementary portions or forms of the Y. Do
25 you see that?

1 A. That's correct.

2 Q. Do you consider the arms of the Y a
3 barcode?

4 (Pause.)

5 A. So Figure 1 is an overview of the
6 duplex sequencing process. The arms of the
7 molecule can certainly serve as a barcode.

8 Q. Is there any limitation to what
9 nucleotide sequences in the adapters would be
10 considered barcode?

11 ATTORNEY POWERS: Object to form.

12 A. I think it would depend on -- I can't
13 answer that question specifically. As I
14 mentioned, a barcode can denote different things.
15 So it would depend on how the barcode was being
16 used. It would depend exactly what you mean by
17 the word "limitation."

18 It's hard to answer that question
19 accurately.

20 Q. You said it would depend on how the
21 barcode's being used?

22 ATTORNEY POWERS: Is there a question
23 pending?

24 Q. Would it be reasonable to randomly
25 select a sequence of nucleotides from the adapter

1 and just call it a barcode?

2 ATTORNEY POWERS: Object to form.

3 A. Can you describe what you mean by
4 "randomly select"?

5 Q. If I take my pen and circle a portion
6 of the adapter, can we call that a barcode?

7 A. So it would certainly depend on what
8 region you would select with your pen, or it could
9 depend on the sequence you select with your pen.

10 Q. Is it possible to select a portion that
11 would not be considered a barcode?

12 A. It would depend on the sequence of the
13 adapter molecule and exactly the context in which
14 the molecular reaction was being applied.
15 Different sequences can serve as barcodes in some
16 contexts but not serve as barcodes in other
17 contexts.

18 Q. If I selected a portion that was not
19 used to identify a molecule, would it be fair to
20 consider it a barcode?

21 ATTORNEY POWERS: Object to form.

22 A. Not necessarily, no. Sorry, actually,
23 before -- I want to make sure I didn't reverse the
24 double negative. Would you mind repeating the
25 question?

1 Q. If I select a portion of the adapter
2 molecule that is not used to specifically identify
3 a molecule, would I consider that a barcode?

4 A. It's possible that it could be
5 considered a barcode even if it doesn't specify an
6 original molecule, but it's also possible that it
7 might not be considered a barcode.

8 Q. So you would consider a sequence of
9 barcode even though it's not used to identify a
10 molecule?

11 A. In some contexts it is possible that
12 the sequence that doesn't -- that a sequence that
13 doesn't identify a molecule could be considered a
14 barcode; but in other contexts it's certainly
15 possible that a sequence which doesn't identify a
16 molecule could not be considered a barcode.

17 Q. What would make it possible to consider
18 it a barcode?

19 ATTORNEY POWERS: Object to form.

20 A. It really depends on the experiment, on
21 the goals of the downstream analysis, and of a
22 specific sample or potentially set of samples that
23 were being analyzed as part of the experiment.

24 It's not possible to accurately answer
25 your question without that context.

1 Q. The context goes to what you said, and
2 that is it's possible for it to be a barcode.

3 So my question is what makes it
4 possible.

5 (Pause.)

6 A. So I wouldn't want to speculate about
7 all possible types of experiments, but it's
8 possible for DNA sequences that -- it's possible
9 for a DNA sequence to serve as a barcode in one
10 context and not serve as a barcode in another
11 context. It just depends on the type of
12 experiment or analysis that's being done.

13 If you'd like to propose a specific
14 type of context, I'm happy to talk through it with
15 you, but I wouldn't want to speculate about any
16 possible experiment.

17 Q. What would you need to know about how a
18 nucleotide sequence is being used in an experiment
19 in order to determine whether or not it's a
20 barcode?

21 A. So I can give some examples. I
22 wouldn't want to say this is a comprehensive list.
23 I would want to know how that nucleic acid
24 sequence was being used in downstream analysis.

25 So often when working with barcodes

1 it's not just the experimental protocol that's
2 relevant but also the downstream analytical steps
3 which describe how that nucleic acid sequence is
4 used and how different steps of the analytical
5 process might take place depending on the sequence
6 that was obtained.

7 I would also want to know what samples
8 were being analyzed as part of that reaction
9 process.

10 Q. Earlier you drew a comparison to a
11 barcode used in I think you said a grocery store.

12 A. Yes.

13 Q. So like a can of soup will have a
14 barcode on it?

15 A. That's correct.

16 Q. And if you go to the counter and scan
17 that barcode, the machine knows you have a can of
18 soup; correct?

19 A. That's correct.

20 Q. And if you scan the wrong side of the
21 soup can, the machine doesn't know you have a can
22 of soup?

23 A. In the context of a can of soup, I
24 would agree with that statement, yes.

25 Q. And if you don't scan the entire

1 barcode, the machine also doesn't know you have a
2 can of soup, because it doesn't read the barcode;
3 right?

4 A. So I am not an expert in the algorithm
5 that the grocery store checkout machines use to
6 link particular products to their database of
7 prices. I was simply giving a broad overall
8 analogy for the fact that a barcode sequence can
9 be used to delineate information.

10 I wouldn't overinterpret that analogy
11 too carefully in the context of some of your
12 questions.

13 Q. There's not a whole lot of
14 overinterpretation. I think what we're getting at
15 is there needs to be a sufficient amount of
16 information to identify the thing being
17 identified; is that fair?

18 ATTORNEY POWERS: Object to form.

19 A. So it's possible that, again -- I can
20 envision a hypothetical situation where a grocery
21 store, for example, has multiple cans of soup that
22 are different colors and different prices but have
23 the same barcode. And I think it would still be
24 possible for the cashier, with the correct amount
25 of information, to be able to delineate the

1 different cans of soup from each other even though
2 they might have the same barcode sequence.

3 Q. But now you're departing from the
4 barcode because you're injecting a human being
5 that is taking in a lot more information than a
6 barcode; right?

7 A. I don't agree with that statement.

8 Q. You mentioned a human being; right?

9 A. Well, it depends to some extent on your
10 definition of a barcode and whether the color of
11 the soup can could be considered part of the
12 barcode.

13 But, again, we're starting to go a
14 little speculative and outside of -- I'm simply
15 pointing out that multiple pieces of information
16 can be used to identify something.

17 Q. Where we're going outside is when you
18 mentioned my definition of a barcode. Do you
19 understand that?

20 ATTORNEY POWERS: Object to form.

21 A. I don't, I'm sorry.

22 Q. Okay. I'm asking your definition of a
23 barcode. What is that?

24 A. So as I think I answered this question
25 earlier as well, but a barcode in the context of

1 DNA sequence analysis is typically used to encode
2 a piece of information. I think that's actually a
3 good definition.

4 Q. Any piece of information?

5 A. It just depends on the context. It's
6 not necessarily any piece of information. It just
7 depends on what the experimenter is trying to do,
8 what's the downstream analysis protocol, what
9 other pieces of information might also be present
10 in the context of the experiment.

11 It's -- it is a broad term, and it's
12 hard to answer accurately in every specific
13 context.

14 Q. In the context of this patent, is it
15 reasonable to select any contiguous set of
16 nucleotides found in the adapter and call that a
17 barcode?

18 ATTORNEY POWERS: Object to scope,
19 form.

20 A. It would depend on specifically what
21 adapter is used. There may be adapter molecules
22 where the entire sequence would represent a
23 barcode, and there may be adapter molecules where
24 that's not true. It would depend.

25 Q. And what would it depend on?

1 A. It would depend on a number of things.
2 And this is not an exhaustive list. But one thing
3 that it might depend on is the sequence, total and
4 complete sequence of the adapter molecule. But
5 the context of the experiment would also matter,
6 and the application and the downstream analysis
7 pipeline would also matter.

8 Q. So really any contiguous set of
9 nucleotides can be considered a barcode?

10 ATTORNEY POWERS: Objection.

11 A. I don't believe that's what I said.

12 Q. So it's not accurate to say that any
13 set of contiguous nucleotides would be considered
14 a barcode?

15 A. It's essential in answering your
16 question that it depends on the context. There is
17 not a yes or no answer to that question.

18 Q. Could you envision a situation where a
19 contiguous set of nucleotides is not considered a
20 barcode?

21 A. So I don't think my job here is to
22 speculate on every possible experimental context.
23 I just want to again highlight the important --
24 well, the important point which is relevant to my
25 opinion is that whether or not something is

1 considered a barcode will depend on a number of
2 additional factors which are important for
3 context.

4 Q. Your job here is to answer the
5 questions that are being posed to you. Do you
6 understand that?

7 A. I do.

8 Q. My question was could you envision a
9 situation where a contiguous set of nucleotides in
10 an adapter molecule is not considered a barcode.

11 A. Yes, I could envision that situation.

12 Q. What would that situation look like?

13 A. So I'll give one example, but I
14 would -- I'll give one example.

15 Sometimes these adapter molecules are
16 very long. Let's envision a situation where an
17 adapter molecule is 500 bases long. Some portions
18 of that adapter molecule might be subject to DNA
19 sequence analysis, and some portions of the
20 adapter molecule might not be subject to DNA
21 sequence analysis. Not every DNA nucleotide that
22 is present on a molecule is always sequenced when
23 doing next-generation sequencing.

24 So, for example, there may be
25 nucleotides that are part of the adapter molecules

1 that are never subject to DNA sequence analysis.
2 Those nucleotides could therefore never be
3 considered part of downstream analytical steps
4 because no data on their sequence content would be
5 generated as part of the DNA sequencing process.

6 Q. Okay.

7 A. I don't see how -- that's an example of
8 a situation where a particular set of nucleotides
9 that are present on an adapter molecule would not
10 qualify as a barcode.

11 Q. Could you envision a situation where a
12 contiguous set of nucleotides in an adapter
13 molecule that is subject to sequencing is not
14 considered a barcode?

15 (Pause.)

16 A. Again, I hesitate to speculate. You
17 keep adding sort of restrictions and limitations
18 to this -- to this question. I'm just hesitant to
19 speculate beyond the most important point, which
20 is that a DNA sequence can serve as a barcode in
21 some contexts but not others.

22 Q. That doesn't answer the question.

23 A. Yes, I can envision a situation where
24 there is a DNA sequence that is subject to
25 sequencing analysis that would not be considered a

1 barcode.

2 Q. And what are you envisioning?

3 A. So, for example, we can also
4 specifically think of a barcode in the context of,
5 for example, the claims here. If I look at Claim
6 1, what's stated is that the adapters comprise
7 barcodes selected from a plurality of distinct
8 barcode sequences, suggesting that there are
9 multiple distinct barcode sequences that are
10 present in a nucleic acid sample.

11 As I mentioned previously, adapter
12 molecules can be very long, and I can envision
13 examples where there may be millions of DNA
14 oligonucleotides that are present in a sample but
15 that in one part of the structure for every
16 molecule the DNA nucleic acid sequence is fixed.

17 In that case there would not be a
18 plurality of distinct sequences in that sample,
19 and so that region of the nucleic acid would not
20 constitute a barcode.

21 Q. You said a plurality of distinct
22 sequences in the sample?

23 A. So what I meant was that there might be
24 a million different -- there could be 3,000 bases
25 long, and each of those molecules, when viewing

1 the entire 3,000 base pair sequence, may not be
2 the same.

3 But there may be regions of those
4 molecules where the nucleic acid sequence content
5 is fixed, and in those regions that would not
6 comprise a plurality of distinct barcode sequences
7 because there was only one option in the entire
8 group of molecules being analyzed.

9 Q. You're envisioning a plurality of
10 barcodes as being present in the sample? Did I
11 understand that correctly?

12 A. No, I don't believe so.

13 Q. Where are you envisioning a plurality
14 of different barcodes being present?

15 A. So you asked me for the opposite. You
16 asked me for a situation where a series of
17 nucleotides would not serve as a barcode.

18 Q. Right. I'm asking a specific question
19 based on what you said. You mentioned -- I'm
20 reading from the transcript -- a plurality of
21 distinct sequences in that sample?

22 A. So that wasn't referring to barcode
23 sequences. That was saying there could be many
24 genes that are sequenced or many different DNA
25 molecules being sequenced. That's what I was

1 referring to by a plurality of overall sequences.

2 Q. But you're quoting language from Claim
3 1 talking about a plurality of distinct barcode
4 sequences?

5 A. And I'm -- that's correct. And what
6 I'm saying is that in this hypothetical sample
7 that you've asked me to generate there is a
8 region -- let's say it's nucleotides 200 to 207 --
9 where the nucleotide content is fixed for all the
10 molecules and the sample.

11 So from bases 200 to 207, there is not
12 a plurality of sequences that are present in the
13 sample. There is only one sequence. Therefore
14 the bases 200 to 207 would not meet the claim's
15 definition of a barcode sequence selected from a
16 plurality of distinct barcode sequences because
17 there's no plurality of distinct barcode
18 sequences.

19 Q. Okay. You keep mentioning a
20 hypothetical I am envisioning. That's not
21 correct, is it?

22 ATTORNEY POWERS: Object to form.

23 Q. Answer. Is that correct? Am I the one
24 envisioning a hypothetical here?

25 A. You are the one that asked me to

1 provide you with a potential hypothetical context.

2 Q. And your answer was, Yes, I can
3 envision a situation where there is a DNA sequence
4 that is subject to sequencing analysis that would
5 not be considered a barcode.

6 A. That's correct. I am the one
7 envisioning this hypothetical situation, but I am
8 envisioning it because you asked me to provide an
9 example.

10 Q. You view that as an unfair question?

11 ATTORNEY POWERS: Objection,
12 argumentative.

13 A. I don't believe that I said it was an
14 unfair question.

15 Q. You mentioned Claim 1; right?

16 A. I did, that's correct.

17 Q. Where in Claim 1 does it tell you how
18 it's using a barcode?

19 (Pause.)

20 A. Just to let you know, I'm going to ask
21 for a bathroom break. I'll of course answer the
22 question, but I just wanted to let you know.

23 Q. Thank you.

24 (Pause.)

25 A. So Claim 1, in Claim 1(a), for example,

1 highlights that in order to -- that this is a
2 method of sequencing DNA that requires double-
3 stranded adapter DNA molecules wherein the
4 adapters comprise barcodes.

5 Q. My question is does Claim 1 recite how
6 that barcode is being used.

7 A. So there are a variety of claims in
8 this patent.

9 Q. I'm asking about Claim 1.

10 (Pause.)

11 A. So while Claim 1 defines and highlights
12 the necessity of including a barcode selected from
13 a plurality of distinct barcode sequences in the
14 claim language, there are other claims in the
15 patent that specifically describe how that barcode
16 sequence can be used which depend on Claim 1.

17 Q. And I'm asking about Claim 1. Does
18 Claim 1 recite how the barcode is being used?

19 (Pause.)

20 A. So Claim 1, for example, in is it
21 subclaim or part A defines the need for adapters
22 that comprise barcodes. In other parts of the
23 claim, they highlight, in the context of the
24 overall specification, that, for example, for at
25 least some of the adapter DNA molecules comprising

1 barcodes that you must confirm the presence of at
2 least one sequence read derived from each of the
3 original first and second strands of the adapter
4 DNA molecules.

5 Q. But it doesn't say that's being done
6 using the barcode.

7 A. So as I mentioned, there are multiple
8 points in this document that describe exactly how
9 the barcode is used that includes the overall
10 specification where there are specific teachings
11 for how to use the barcode sequences to be able to
12 determine first and second strand reads but also
13 other claims that very specifically require
14 specific use of the barcode.

15 Q. By "this document" you're referring to
16 the '127 patent?

17 A. That's correct.

18 Q. Okay. And you have -- in order to
19 understand this aspect of Claim 1, you're saying
20 you have to turn to other portions of the
21 document?

22 ATTORNEY POWERS: Objection, misstates.

23 A. I don't believe I said that.

24 Q. You agree that Claim 1 itself does not
25 state how the barcode is being used?

1 ATTORNEY POWERS: Objection, misstates.

2 A. So I'm just going to have to -- I'll
3 have to answer the question in a similar way, that
4 Claim 1(a) defines that the barcode sequence is
5 present or comprised on the adapter molecule, that
6 it's selected from a plurality of distinct barcode
7 sequences.

8 Claim 1(d) requires that for at least
9 some of the -- only the adapter DNA molecules that
10 comprise barcodes that it's important to
11 confirm -- required to confirm the presence of at
12 least one sequence read deriving from the first
13 strand and one sequence read deriving from the
14 second strand. Those come from the barcoded
15 adapter DNA molecules.

16 And then I am also saying there are
17 multiple additional points in this document that
18 provide substantial context on how the barcodes
19 are labeling individual strands and that there are
20 additional claims in this document that
21 specifically require exact uses of the barcode in
22 different contexts.

23 Q. And those exact uses you're referring
24 to are not recited expressly in Claim 1; is that
25 correct?

1 ATTORNEY POWERS: Object to form.

2 A. So there is different language
3 certainly in the different claims. But, again,
4 Claim 1 describes the use of barcode sequences,
5 requires that at least some of the adapter DNA
6 molecules that comprise barcodes are used to
7 confirm the presence of at least one sequence read
8 deriving from the first strand and one sequence
9 read deriving from the second strand.

10 Q. You said there's different language in
11 different claims; is that correct?

12 A. To be more accurate, different claims
13 have different words.

14 ATTORNEY POWERS: Take a break?

15 THE WITNESS: I'd like to break.

16 ATTORNEY ROSATO: Yeah.

17 (Recess taken from 11:26 to 11:35TIME.)

18 Q. Let's turn back to Figure 1 of the '127
19 patent, and let me know when you're there, please.

20 A. Okay. Thank you.

21 Q. Figure 1 recites the term "PCR." Do
22 you see that?

23 A. I do see that.

24 Q. What is PCR?

25 A. PCR is an acronym for the molecular

1 biology reaction polymerase chain reaction.

2 Q. And PCR is an amplification method; is
3 that correct?

4 A. That's correct.

5 Q. Does Claim 1 of the '127 patent recite
6 an amplification step?

7 A. Yes.

8 Q. As does Claim 22; correct?

9 A. That's correct.

10 Q. Do you understand the '127 patent
11 claims as being limited to PCR-based
12 amplification?

13 (Pause.)

14 A. No, I do not.

15 Q. Let's turn back to Figure 1 of the '127
16 patent, please.

17 A. Okay.

18 Q. Figure 1 at the bottom recites
19 massively parallel sequencing. Do you see that?

20 A. I do see that.

21 Q. What is massively parallel sequencing?

22 A. So massively parallel sequencing is a
23 form of nucleic acid analysis. Typically it
24 refers to analyzing a plurality of DNA
25 oligonucleotides and determining the DNA sequence

1 for those oligonucleotides at the same time.

2 Q. Does massively parallel sequencing
3 occur on the Illumina sequencing platform?

4 A. The Illumina -- the biotechnology
5 company Illumina does offer the product, a number
6 of machines and kits, that enable massively
7 parallel sequencing.

8 Q. Does cluster amplification occur on the
9 Illumina sequencing platform?

10 A. Many of the sequencing instruments
11 offered by Illumina do utilize a cluster
12 amplification step when performing massively
13 parallel sequencing.

14 Q. And do you understand the claims of the
15 '127 patent to be limited to sequencing on the
16 Illumina sequencing platform?

17 A. No.

18 Q. Let's turn to the abstract of the '127
19 patent, and let me know when you're there.

20 A. Okay.

21 Q. There's a sentence in the abstract that
22 reads, To overcome limitations in sequencing
23 accuracy, a method duplex consensus sequencing,
24 DCS, is provided.

25 Do you see that?

1 A. I do see that.

2 Q. Let's turn to Column 16 of the '127
3 patent. Let me know when you're there.

4 A. Do you mind if I take a minute to read
5 it?

6 Q. Of course not.

7 (Pause.)

8 A. Okay. Thank you.

9 Q. Column 16, lines 19 through 28 reads,
10 The method of generating an error-corrected
11 double-stranded contiguous sequence further
12 comprises the second strand that is termed DCS.
13 The DCS stage includes steps of comparing the
14 sequence of the two single-strand contiguous
15 sequences arising from a single-duplex DNA
16 molecule and further reducing sequencing or PCR
17 errors by considering only sites at which the
18 sequences of both single-stranded DNA molecules
19 are in agreement.

20 Do you see that?

21 A. I do see that.

22 Q. I corrected a typo, if you didn't
23 notice.

24 A. It says "stance" instead of "strand"?
25 Is that what you meant?

1 Q. Yes. Thank you for noticing that.

2 The last sentence in that paragraph
3 states, the method that includes both the first
4 stage and second stage termed duplex consensus
5 sequencing, DCS.

6 Do you see that?

7 A. I do see that.

8 Q. The paragraph above refers to the first
9 stage termed single-strand contiguous sequencing.
10 Do you see that?

11 A. I do see that term.

12 Q. And that sentence continues, followed
13 by a second stage of duplex consensus sequencing,
14 DCS.

15 Do you see that?

16 A. I do see that.

17 Q. Let's turn back to Figure 1 of the '127
18 patent.

19 A. Okay.

20 Q. Does Figure 1 depict a single-strand
21 contiguous sequence?

22 (Pause.)

23 A. I don't believe so, no.

24 Q. Does Figure 1 depict comparing one
25 single-strand contiguous sequence to another

1 single-strand consensus sequence?

2 A. I don't believe so, no.

3 Q. Let's look at the '127 patent claims
4 starting with Claim 1. Let me know when you're
5 there.

6 A. Okay.

7 Q. Does Claim 1 recite the term "consensus
8 sequence"?

9 A. I don't see the words "consensus
10 sequence" appearing in Claim 1.

11 Q. Let's turn to Claim 22. Let me know
12 when you're there.

13 A. I'm there.

14 Q. Step D of Claim 22 recites comparing
15 the consensus sequence to reference sequence.

16 Do you see that?

17 A. I do see that.

18 Q. Does Claim 22 recite comparing one
19 single-strand consensus sequence to another
20 single-strand consensus sequence?

21 (Pause.)

22 A. Can you repeat the question?

23 Q. Does Claim 22 recite comparing one
24 single-strand consensus sequence to another
25 single-strand consensus sequence?

1 A. So Claim D references collapsing a
2 plurality of strand sequence reads within the
3 families to provide a consensus sequence for each
4 of at least some of the double-stranded DNA
5 molecules in the library.

6 Q. Okay. And the next step is comparing
7 the consensus sequence to a reference sequence;
8 correct?

9 A. That's correct. But the claim does not
10 specify that that's a single-strand consensus
11 sequence.

12 Q. Okay. So my original question was does
13 Claim 22 recite comparing one single-strand
14 consensus sequence to another single-strand
15 consensus sequence. It sounds like the answer is
16 no.

17 A. So a person of ordinary skill in the
18 art would recognize that an overall consensus
19 sequence from a nucleic acid could be obtained by
20 comparing a single-stranded consensus sequence
21 from one strand to a single-stranded consensus
22 sequence from another strand.

23 Q. And does Claim 22 recite that?

24 A. Claim 22 recites, collapsing a
25 plurality of strand sequence reads within the

1 families to provide a consensus sequence for each
2 of at least some of the double-stranded DNA
3 molecules in the library.

4 It does not limit that to single-strand
5 consensus sequence.

6 Q. Nor does it recite comparing one
7 single-strand consensus sequence to another
8 single-strand consensus sequence; right?

9 A. So, as I said, one -- a person of
10 ordinary skill in the art would recognize that one
11 way to provide a consensus sequence for each of at
12 least some of the double-stranded DNA molecules in
13 the library would be to compare -- would be to
14 first collapse a plurality of strand sequence
15 reads into single-strand consensus sequences and
16 then to compare those two sequences.

17 Q. But that way is not recited in Claim 1?
18 Excuse me. Claim 22?

19 ATTORNEY POWERS: Object to form.

20 A. So Claim 22 highlights the possibility
21 of collapsing a plurality of strand sequence reads
22 within the families to provide a consensus
23 sequence. A person of ordinary skill in the art
24 would recognize that one of the ways to obtain a
25 single-strand consensus sequence would be to

1 collapse a plurality of strand sequence reads.

2 A person of ordinary skill in the art
3 would also recognize that to meet the limitation
4 of 22(d), which is to provide a consensus sequence
5 for each of at least some of the double-stranded
6 DNA molecules in the library, one way of doing
7 that would be to compare two single-stranded
8 consensus sequences.

9 Q. Earlier you stated Claim 22 does not
10 specify that that's a single-strand consensus
11 sequence. Do you remember saying that?

12 A. The words "single-stranded consensus
13 sequence" is not in Claim 22.

14 Q. Okay. And in the comparing step in
15 Step D of 22, the word "reference sequence" is in
16 that step; correct?

17 A. That's correct.

18 Q. Let's turn to paragraph 85 of your
19 declaration. Let me know when you're there.

20 (Pause.)

21 A. I'm there.

22 Q. At the bottom of paragraph 85 you
23 state, Guardant argued that index barcodes are
24 different from molecular barcodes. I agree.

25 Do you see that?

1 A. I do see that.

2 Q. Previously in paragraph 83 you indicate
3 that sample barcodes are also known in the art as
4 index barcodes; is that right?

5 A. That's correct.

6 Q. Terminology is helpful. Thank you.

7 Are sample barcodes also referred to as
8 multiplexing barcodes?

9 A. They can be but -- sometimes people use
10 different words to refer to different things. It
11 usually is helpful to see the overall context of
12 how the word is being used.

13 For example, typically in the art the
14 word "sample barcode" and "index barcode" mean the
15 same thing, but there are cases where people use
16 "index barcode" in a different way. But that will
17 usually be clear by looking at the overall context
18 of the reference.

19 Q. What is a multiplexing step? What does
20 multiplexing mean?

21 A. So "multiplexing" is a broad term that
22 can mean different things depending on the
23 context. But typically it refers to the idea of
24 doing multiple things at the same time. But what
25 those things are will depend on the context of the

1 reference and the specific analysis being
2 conducted.

3 Q. Is the term "multiplexing" used for the
4 context of looking at multiple different samples
5 in one reaction?

6 A. It certainly can be. And different
7 samples, for example, may refer to different DNA
8 material from different human beings, just as an
9 example.

10 Q. So down in paragraph 84, the third
11 sentence, you state, Indexing barcodes or sample
12 barcodes are short unique sequences of DNA added
13 to all molecules from a specific sample so samples
14 can be pooled, then processed and sequenced in
15 parallel, with each resulting sequence containing
16 information to determine the source material
17 starting sample.

18 Do you see that?

19 A. I do see that.

20 Q. My question goes to the word "short."
21 What is a short sequence?

22 ATTORNEY POWERS: Object to form.

23 A. So I don't provide a specific number of
24 nucleotides. DNA sequences can go from one base
25 pair to hundreds of millions of base pairs, for

1 example, on a human chromosome. Typically in the
2 art indexing barcodes will be between 4 and 30
3 nucleotides. There can be exceptions to that.

4 The important thing is that those
5 indexing barcodes enable material from different
6 sources to be pooled together and then effectively
7 indexed after the sequencing data is collected so
8 that each molecule can be returned back or grouped
9 together with molecules from the same original
10 source, for example, human being.

11 Q. You used the term "molecular
12 barcode" -- is that correct? -- in your
13 declaration?

14 A. I do.

15 Q. A molecular barcode is a barcode;
16 correct?

17 A. That's correct.

18 Q. And a sample barcode is a barcode?

19 A. A molecular barcode and sample barcodes
20 are -- or index barcodes are different things.

21 Q. Are they barcodes?

22 A. So we had a discussion earlier about
23 whether something could be considered a barcode,
24 and I said that it will depend on the context. So
25 there are cases where, for example, an index

1 barcode may not be a barcode. It depends on the
2 context.

3 Q. Let's look at the context of your
4 statement in paragraph 84, that sentence we read
5 that begins, indexing barcodes or sample barcodes.
6 Do you see that?

7 A. Uh-huh.

8 Q. In that context is an indexing barcode
9 a barcode?

10 A. Yes.

11 Q. And in that context is a sample barcode
12 a barcode?

13 A. Oh, I'm sorry, I didn't hear the -- I
14 didn't hear your first question properly. Your
15 first question was -- I'd like to modify my
16 answer. Can you read back the previous question?
17 I believe it was in that context is the indexing
18 barcode a barcode; is that right?

19 Q. So we're looking at your statement in
20 paragraph 84, the sentence we read previously that
21 begins, indexing barcodes or sample barcodes.

22 A. That's right.

23 Q. Do you see that sentence?

24 A. That's right.

25 Q. In the context of that sentence, is an

1 indexing barcode a barcode?

2 A. It would depend on the experiment being
3 performed.

4 Q. Well, you're calling them barcodes in
5 that sentence.

6 A. Yes, but the sentence goes beyond the
7 words that you read.

8 Q. And my question is in that context is
9 an indexing barcode a barcode.

10 A. So, for example, I say indexing
11 barcodes; and then I go on to say, so samples can
12 be pooled and then processed and sequenced in
13 parallel with each resulting sequence containing
14 information to determine the source material
15 starting sample.

16 So that sentence is making an
17 assumption that this -- or referring to a
18 particular context that this is an experiment
19 where material from different starting samples is
20 being considered together.

21 So under that assumption where multiple
22 different source material is being pooled together
23 from different original sources and each --
24 material from each individual source is labeled
25 with a different index sequence, then in that

1 specific context the indexing barcode is a barcode
2 of the original source material.

3 Q. And you're calling an indexing barcode
4 a barcode?

5 A. With a specific set of assumptions
6 about how the experiment was performed.

7 Q. Isn't the assumption baked into your
8 own term, "indexing barcode"?

9 A. As I've said, in some contexts a
10 nucleic acid sequence can serve as a barcode, and
11 in other contexts it can't. It depends on the
12 experiment, the goals of the analysis, and the
13 samples being analyzed.

14 Q. So you used the term "indexing
15 barcode"; is that correct?

16 A. For example, I say in paragraphs 84
17 that the use of indexed barcoded samples is very
18 different from the claim step of grouping the
19 strands of sequence reads into families based on
20 the barcode and DNA fragment-specific information.

21 Q. And that's not what I'm asking you, is
22 it?

23 ATTORNEY POWERS: Object to form.

24 A. You asked me if I used the term
25 "indexed barcode."

1 Q. Yes. That was the question.

2 A. And I'm saying in that sentence I do
3 use the term "indexed barcode" and continue to
4 draw opinions based on that term to highlight that
5 those barcodes are very different than what is
6 included in the claim step.

7 Q. Paragraph 83 used the term "indexed
8 barcodes"; correct?

9 A. In paragraph 83 I also used the term
10 "indexed barcode" in a similar context
11 highlighting that the use of indexed barcodes is
12 to track sample origins and not to group strands
13 into families based on barcode sequence and DNA
14 fragment specific information.

15 Q. And the term "indexed barcodes"
16 includes the word "barcodes"; correct?

17 A. I would agree with that statement.

18 Q. Okay. Thank you. It doesn't have to
19 be that hard.

20 Okay. Let's look at Column 20, lines
21 40 through 41 of the '127 patent, and let me know
22 when you're there.

23 A. Can you remind me which section again,
24 please?

25 Q. So Column 20, lines 39 through 40. Do

1 you see where it states, XXXXXX indicates the
2 position of a fixed multiplexing barcode sequence?

3 A. I'm just going to read the section
4 alone for one second, sorry.

5 (Pause.)

6 A. Okay. Thank you.

7 Q. So do you see the sentence XXXXXX
8 indicates the position of a fixed multiplexing
9 barcode sequence?

10 A. I do see that.

11 Q. And are you aware that this is the only
12 mention of the term "barcode" in the entire '127
13 specification?

14 ATTORNEY POWERS: Object to form.

15 A. So we've discussed earlier about how a
16 person of ordinary skill in the art would bring
17 their expertise and knowledge and relevant
18 knowledge of pertinent art in the field when
19 reading a specification.

20 We've also talked about how sometimes
21 people use slightly different words to refer to
22 the same thing. For example, in my lab we often
23 work with a construct known as a UMI, which is an
24 abbreviation for unique molecular index. That
25 term is used interchangeably with the term

1 "molecular barcode." And the papers that we
2 write, we can use those terms effectively
3 interchangeably.

4 And I mention that because it
5 highlights that in the art sometimes the word
6 "barcode" and the word "index" can get used to
7 mean the same thing. And that gets a little
8 complicated because there's also the term "index
9 barcode," which refers to sample barcode. But we
10 understand that in the right context a person of
11 ordinary skill in the art will understand what
12 these terms are referring to.

13 So I would highlight that the term
14 "SMI," which is single-molecule identifier --
15 "identifier," and "index" are also example of
16 terms that are associated with barcode -- appears
17 many times in the specification.

18 So a person of ordinary skill in the
19 art would understand that the authors were talking
20 about DNA sequences that encoded specific types of
21 information, even if they don't always use the
22 word "barcode."

23 Q. This reference in the '127
24 specification to a multiplexing barcode sequence,
25 are you saying that that's an SMI sequence?

1 A. I am absolutely not saying that that is
2 an SMI sequence.

3 Q. But it's stated here as a barcode
4 sequence; correct?

5 A. The word "barcode" is included in that
6 sentence, but what I want to highlight is that
7 other words which have -- are meant to represent
8 the same molecular biology context, in particular
9 the word "identifier," also appear at multiple
10 points in the specification.

11 Q. And are you saying there are other
12 examples of barcodes in the specification?

13 A. That is what -- yes, that's correct.

14 Q. Got it. Okay.

15 ATTORNEY ROSATO: Why don't we break
16 here.

17 ATTORNEY POWERS: Sounds fine.

18 (Time noted: 12:08 p.m.)

19

20

21

22

23

24

25

1 A F T E R N O O N S E S S I O N

2 (Time noted: 12:53 p.m.)

3 R A H U L S A T I J A ,

4 resumed as a witness, having been previously
5 sworn by the notary public, was examined and
6 testified further as follows:

7 EXAMINATION CONTINUED BY

8 ATTORNEY ROSATO:

9 Q. Let's turn to the claims of the '127
10 patent. Let me know when you're there, please.

11 A. Okay. I'm there.

12 Q. Claim 13 references both Y-shaped and
13 U-shaped adapters. Do you see that?

14 A. I do see that.

15 Q. Claim 10 recites, amplifying original
16 strands via PCR amplification, cluster
17 amplification, rolling circle amplification, or a
18 combination thereof.

19 ATTORNEY POWERS: Object to form.

20 Q. Do you see that?

21 ATTORNEY POWERS: Misstates the
22 document.

23 A. Could you repeat the question?

24 Q. Yes. Claim 10 recites, quote,
25 amplifying original strands via PCR amplification,

1 cluster amplification, rolling circle
2 amplification, or a combination thereof, end
3 quote.

4 Do you see that?

5 A. I do see that.

6 Q. Paragraph 214 of your declaration you
7 discuss the '127 patent's rolling circle
8 replication embodiment. Do you see that?

9 A. I do see that.

10 Q. The last sentence in paragraph 214 you
11 state, The '127 patent's claimed embodiment in
12 Claim 10 is not limited to Travers's '075 rolling
13 circle replication embodiment.

14 Do you see that?

15 A. Yes, I do.

16 Q. In the next paragraph, paragraph 215,
17 you cite to Column 11, lines 15 through 18 of the
18 '127 patent. Do you see that?

19 A. I do see that.

20 Q. And the content you quote is
21 recognition sites for restriction endonuclease
22 digestion could be engineered into these
23 adapters...if more convenient for subsequent
24 steps.

25 Do you see that quote?

1 A. I do see that.

2 Q. A few lines down you state that Travers
3 '075 and Travers 2010 do not disclose any of these
4 downstream modification stepped disclosed in '127.

5 Do you see that?

6 A. I do see that.

7 Q. By "these downstream modification
8 steps" are you referring to the recognition sites
9 for restriction endonuclease digestion that you
10 cite above?

11 A. Sorry, I just was reading through. Do
12 you mind repeating the question?

13 Q. So at the top of the page you are
14 citing to recognition sites for restriction
15 endonuclease digestion; correct?

16 A. That's correct.

17 Q. A few lines down you state, Travers
18 '075 and Travers 2010 do not disclose any of these
19 downstream modification steps.

20 A. That's correct.

21 Q. Do you cite any citations here to
22 Travers '075 and Travers 2010?

23 A. In that sentence there are no
24 additional citations in that sentence of my
25 report.

1 Q. Let's get you copies of Travers, both
2 Travers. So I am handing you a copy of Exhibit
3 1018, the Travers '075; correct?

4 A. This is '075. Did you provide both?

5 Q. Not yet.

6 A. That's fine.

7 Q. I'm doing them one at a time. This is
8 Exhibit 1021. That's the Travers 2010.

9 That's Travers 2010; correct?

10 A. The Nucleic Acids research article I
11 referred to as Travers 2010.

12 Q. Can you turn to paragraph 80 of Travers
13 2010 and let me know when you're there.

14 (Pause.)

15 A. Okay.

16 Q. Paragraph 80 of Travers '075 states, In
17 some cases it may be desirable to provide
18 endonuclease recognition sites within the linking
19 oligonucleotide which can allow for a mechanism to
20 release a given template sequence from a synthesis
21 reaction, i.e., by linearizing it and allowing the
22 polymerize to run off the linear template and/or
23 to expose the template to endonuclease activity
24 and thus terminate synthesis through removal of
25 the template.

1 Such sites could additionally be
2 excluded as control sequences by providing
3 specific binding locations for endonucleases
4 engineered to lack cleavage activity but retain
5 sequence-specific binding.

6 Did I read that correctly?

7 A. I don't believe so, but I think -- but
8 with a minor exception.

9 Q. Do you want to repeat the whole
10 paragraph?

11 A. Sure. Do you want me to start from
12 paragraph 80? In some cases it may be desirable
13 to provide endonuclease recognition sites within
14 the linking oligonucleotide which can allow for a
15 mechanism to release a given template sequence
16 from a synthesis reaction, i.e., by linearizing it
17 and allowing the polymerase to run off the linear
18 template and/or to expose the template to
19 endonuclease activity and thus terminate synthesis
20 through removal of the template.

21 Such sites could additionally be
22 exploited as control sequences by providing
23 specific binding locations for endonucleases
24 engineered to lack cleavage activity but retain
25 sequence-specific binding.

1 Q. Thank you.

2 Can you look above to paragraph 78.

3 The bottom of paragraph 78 recites, Likewise, an
4 engineered pause point within the linking
5 oligonucleotide region could include a damaged
6 base that causes a stop in replication until
7 repair enzymes are added to the mixture; for
8 example, the linking oligonucleotide could be
9 included, a base position having a pyrimidine
10 dimer.

11 Such compounds would cause the
12 replication complex to pause. Addition of the
13 photolyase DNA repair enzyme would repair the
14 problem location and allow replication sequencing
15 to continue.

16 Do you see that?

17 A. Yes, I see that.

18 Q. Can you look at Claim 11 of the '127
19 patent?

20 A. Okay.

21 Q. Does your declaration provide a
22 comparison between Claim 11 and paragraph 78 of
23 Travers?

24 ATTORNEY POWERS: Object to form.

25 A. Can you say what you mean by "a

1 comparison" or "provides a comparison"?

2 Q. Does your declaration ever cite to
3 paragraph 78 of Travers?

4 A. So I don't want to read through every
5 page of the declaration, even though I'd like to
6 speak accurately. I can't think of an instance at
7 the moment in my declaration where I cite to
8 paragraph 78 of Travers.

9 Q. Let's turn to page 26 of your
10 declaration. Let me know when you're there.

11 A. Okay. I'm here.

12 Q. So paragraph 42 at the bottom of the
13 page states, The Travers '075 teaches that the
14 sequencing methods do not amplify the templates
15 before sequencing. And there's a citation
16 specifically to paragraph 122 of Travers '075.

17 Do you see that?

18 A. Sorry, if you could repeat the
19 question. I was just -- I got lost.

20 Q. Paragraph 42 in the first -- excuse me,
21 in the second sentence states that Travers '075 --
22 excuse me. Strike that and start over.

23 Paragraph 42 of your declaration
24 states, Travers '075 also teaches that the SMRT
25 sequencing methods do not amplify the SMRTbell

1 templates before sequencing.

2 Do you see that?

3 A. That's correct.

4 Q. The next sentence in paragraph 42 cites
5 to paragraph 122 of Travers '075; correct?

6 A. Yes, that's correct.

7 Q. Can you turn to Travis '075, paragraph
8 122. You seem to be better reading these than I
9 am --

10 A. No, I'll let you. Please go ahead.

11 Q. Why don't you go ahead and read aloud
12 what's stated in paragraph 122.

13 A. So I am simply reading the words under
14 paragraph 122.

15 Although the constructs of the
16 invention are described primarily and preferably
17 for use directly as templates for, e.g.,
18 sequencing application, it will be appreciated
19 that the structures may also serve as intermediate
20 structures in the preparation of templates that
21 provide for sequence redundancy in line with that
22 provided by such constructs.

23 For example, the structurally circular
24 nucleic acid segments described herein may be used
25 as templates in a rolling circle replication

1 process to produce concatemer molecules that
2 include repeating copies of both the sense and
3 antisense strands of the originating
4 double-stranded segment included within the
5 circular nucleic acid.

6 These replicated products may then be
7 employed directly as template molecules in a
8 template-dependent sequencing process as described
9 elsewhere herein. See also U.S. patent number
10 7,476,503, which is incorporated herein by
11 reference in its entirety for all purposes.

12 Likewise, duplication processes may be
13 employed to produce multiple copies of a prepared
14 circular construct using methods previously
15 described. See, e.g., U.S. patent application
16 number 61-072160, previously incorporated herein
17 by reference in its entirety for all purposes.

18 And I'd like to highlight again for the
19 record that in both this paragraph and in the
20 previous question that you asked me I was simply
21 reading from the Travers '075 specification.

22 Q. Appreciate that.

23 So in paragraph 42 of your declaration
24 are you quoting the full content of paragraph 122
25 of Travers?

1 A. In paragraph 42 of my declaration, I do
2 not quote the entirety of paragraph 122 of
3 Travers, but I believe that my statement
4 accurately reflects the paragraph.

5 Q. It's your position that paragraph 122
6 of Travers does not discuss amplifying the
7 template before sequencing?

8 A. That's not what I said.

9 Q. I'm asking. Is it your position that
10 paragraph 122 of Travers '075 does not discuss
11 amplifying the template before sequencing?

12 A. The paragraph includes the words
13 "rolling circle of replication," but it does not
14 teach an embodiment for how to perform -- it does
15 no teach how to perform such an embodiment.

16 Q. That's not my question. My question is
17 does it discuss amplification prior to sequencing.

18 A. So, as I said before, in paragraph 122
19 of Travers '75, as I read, the words may be used
20 as templates in a rolling circle replication
21 process to produce concatemer molecules that
22 include repeating copies of both the sense and
23 antisense strands of the originating
24 double-stranded segment, including -- included
25 within the circular nucleic acid.

1 These replicated products may then be
2 employed directly as template molecules in a
3 template dependent sequencing process as described
4 elsewhere therein.

5 Those words appear in the paragraph.

6 However, as I say in my declaration,
7 Travers '075 does not teach how to perform this
8 embodiment.

9 Q. And when you say it doesn't teach how
10 to perform it, you mean it's not laying out all
11 the details of every step?

12 A. That's not exactly what I mean.

13 Q. Well, you agree that it discusses in
14 this paragraph amplification prior to sequencing;
15 correct?

16 A. I agree that the words "rolling circle
17 replication" appear in this paragraph, but I do
18 not agree that Travers '075 teaches how to perform
19 this embodiment.

20 Q. You're saying two different things.
21 I'm asking if it's discussed in this paragraph.
22 It sounds like your answer is yes, it's discussed.

23 A. So, again, the words "rolling circle
24 replication" appear in paragraph 122. But as I
25 say in my declaration, Travers '075 does not teach

1 how to perform rolling circle replication prior to
2 performing SMRT sequencing.

3 Q. And your position is that the '127
4 patent does teach how to perform rolling circle
5 prior to amplification?

6 ATTORNEY POWERS: Objection, form,
7 cope.

8 (Pause.)

9 A. Can you repeat the question? Sorry.

10 Q. Is it your position that the '127
11 patent does teach how to perform rolling circle
12 amplification prior to sequencing?

13 ATTORNEY POWERS: Same objections.

14 A. Thank you.

15 I want to highlight that you're asking
16 two different questions.

17 Q. I'm asking one question right now. You
18 can focus --

19 ATTORNEY POWERS: Please don't
20 interrupt the witness.

21 Please continue your answer.

22 THE WITNESS: Yes.

23 Q. Let me repeat the question. The
24 question is is it your position that the '127
25 patent does teach how to perform rolling circle

1 amplification prior to sequencing.

2 A. In your previous question you asked
3 essentially the same thing in regards to Travers
4 '075. And what I'd like to highlight is that
5 these are two different issues at play. In
6 Travers '075 -- we can go back to paragraph 122.

7 Q. I'm going to have to instruct you to
8 answer the question.

9 A. I will.

10 ATTORNEY POWERS: Don't interrupt the
11 witness, Mike.

12 Q. I'm asking about the '127 patent.

13 ATTORNEY POWERS: Please don't
14 interrupt the witness.

15 ATTORNEY ROSATO: I'm going to ask the
16 witness to answer the question that is posed
17 and not dodge it and answer a different
18 question. Your objection is noted, counsel.

19 ATTORNEY POWERS: HE'S trying to
20 answer, and I will have the witness give his
21 full answer. Thank you.

22 ATTORNEY ROSATO: I ask the court
23 reporter to read back the question that's
24 pending.

25 (Record read.)

1 A. I'd like to give the full context for
2 my answer. Thank you.

3 So, as I was saying, in the Travers '75
4 patent, when rolling circle replication is
5 discussed it is discussed in a particular context,
6 that these replicated products may then be
7 employed directly as template molecules in a
8 template-dependent sequencing process as described
9 elsewhere herein.

10 It then cites to a U.S. patent number
11 that describes the SMRT sequencing process.

12 In my declaration I highlight that the
13 '127 patent -- excuse me. Let me start that
14 sentence again.

15 In my declaration starting in paragraph
16 214, for example, I highlight that the '127
17 patent's claimed embodiment in Claim 10, which is
18 what you are asking me about, is not limited to
19 the Travers '075 rolling circle replication
20 embodiment. Those are key differences that are
21 relevant to the question you asked.

22 I also highlight that in the '127
23 patent any suitable method known in the art could
24 be used for sequencing. And I also highlight that
25 the '127 patent discloses that recognition sites

1 for restriction endonuclease digestion could be
2 engineered into these adapters if more convenient
3 for subsequent processing steps. Those are key
4 differences with the Travers '75 embodiment.

5 Q. So one key difference you identified
6 was that Claim 10 is not limited to Travers's '075
7 rolling circle replication embodiment; is that
8 correct?

9 A. Just to be absolutely specific, I
10 listed two reasons that followed from that
11 statement. Because it's not limited to the '075
12 rolling circle embodiment, it's possible for a
13 person of ordinary skill in the art to do two
14 things.

15 One is to use any suitable method known
16 in the art for downstream sequencing steps, and
17 the other is to include downstream subsequent
18 processing steps which include introducing
19 recognition sites for restriction endonuclease
20 digestion.

21 Q. Column 15, lines 36 and 37 of the '127
22 patent recites, Pacific Biosciences sequencing
23 platform. Do you see that?

24 A. Sorry, can you remind me of the
25 location?

1 Q. Column 15, lines 36 and 37.

2 A. I see that.

3 Q. Look at Column 10 of the '127 patent.

4 A. I just want to modify my previous
5 answer. You asked me if I saw the words "Pacific
6 Biosciences" in that sentence. I'd want to read
7 the full sentence in context and note that
8 additional sequencing platforms, which include the
9 Illumina sequencing platform, the ABI SOLiD
10 platform, Pacific Biosciences, 454 Life Sciences,
11 Ion Torrent, and Helio sequencing platform are
12 also listed in that paragraph and that earlier in
13 that paragraph the author states that any suitable
14 method known in the art could be used.

15 Q. Okay. Thank you.

16 Turn to Column 10, please, of the '127
17 patent. Let me know when you're there, please.

18 A. Okay. I'm there.

19 Q. Column 10, starting at line 63 reads,
20 Moreover, ligation and amplification with
21 circularizing linkers -- i.e., hairpin linkers
22 affixed to both ends of the fragment -- has been
23 demonstrated as a step in the Pacific Biosciences
24 sample preparation work flow 49.

25 Do you see that?

1 A. I see that.

2 Q. What is reference 49?

3 (Pause.)

4 A. I believe it's the Travers 2010
5 reference.

6 Q. Correct.

7 And the next sentence reads, As the
8 sequence of the linker itself does not matter in
9 the work flow, the published linker sequences from
10 either of these references would be adequate for
11 use in the assay.

12 Do you see that?

13 A. I do see that.

14 Q. And then a few lines down on Column 11
15 starting about line 13 the '127 patent states,
16 Additionally, closed circles may be preamplified
17 using rolling circle amplification or serve as the
18 substrate for continuous loop sequencing, 49.

19 Do you see that?

20 A. I do see that.

21 Q. And 49 again is the Travers 2010
22 publication; correct?

23 A. That's correct.

24 Q. Okay. Back to paragraph 122 of Travers
25 '075. Let me know when you're there.

1 A. I'm there.

2 Q. Paragraph 122 of Travers '075 cites to
3 U.S. patent 7,476,503. Do you see that?

4 A. I do see that.

5 Q. And the '503 patent -- well, let's just
6 give you a copy of that.

7 I'm handing you a copy of what was
8 previously marked as Exhibit 2008. Do you
9 recognize this document?

10 A. I do.

11 Q. And this is for the record U.S. patent
12 7,476,503; correct?

13 A. Yes, that is correct.

14 Q. Thank you.

15 And I'll also note clarification for
16 the record this '503 patent is backed [phonetic]
17 by a patent that is submitted both as 1020 as well
18 as 2008. We're looking at the 2008 exhibit.

19 A. Thank you.

20 Q. Turn to paragraph 204 of your
21 declaration.

22 ATTORNEY POWERS: What paragraph, Mike?

23 ATTORNEY ROSATO: 204.

24 A. Okay. I'm there.

25 Q. You provide two citations in paragraph

1 204 to the '503 patent. Could you identify those
2 citations?

3 (Pause.)

4 A. The first citation is on Column 23,
5 lines 51 through 54, and I cite the sentence:
6 This method also allows the use of target nucleic
7 acid molecules taken directly from a biological
8 sample, minimizing the need for cloning,
9 subcloning, or amplification of the target nucleic
10 acids before sequencing can take place.

11 Q. Thank you.

12 And the second citation is Column 33,
13 lines 24 through 25; correct?

14 A. That's correct. I cite the sentence:
15 In another preferred embodiment, sequencing is
16 performed with polymerases capable of rolling
17 circle replication.

18 Q. Thank you.

19 And there are no additional citations
20 to the '503 patent here; correct?

21 A. In that paragraph I do not list
22 additional citations to the '503 patent.

23 Q. Okay. Do you recall listing any other
24 citations to the '503 patent in your declaration?

25 A. I would have to go through the entire

1 declaration to be certain that I was speaking
2 accurately, but as I sit here at the moment, I
3 cannot -- I don't believe that I make additional
4 citations specifically to the '503 patent.

5 Q. Can you turn to paragraph 91 of your
6 declaration?

7 A. Actually, I just want to add to that
8 answer. Excuse me.

9 While I don't make additional citations
10 to the '503 patent, I do say in paragraph 204 of
11 my report that the '503 patent also does not
12 provide any more detail on how to perform Travers
13 '075 rolling circle replication embodiment.

14 Q. Turn to paragraph 91 of your
15 declaration. Let me know when you're there,
16 please.

17 A. Okay.

18 Q. In the middle of paragraph 91 you
19 state, Travers '075 discloses identifying only the
20 presence of adapter sequences as landmarks or
21 registration sequences that mark the portion of
22 the sequence read where one strand ends and the
23 next begins.

24 Do you see that?

25 A. Yes, I see that.

1 Q. By "registration sequences" are you
2 referring to sequences in Travers's adapter
3 molecule?

4 (Pause.)

5 A. So just to be precise, in paragraph 54
6 of Travers '75 it states, The presence of a
7 linking sequence also provides an opportunity to
8 provide a registration sequence that permits the
9 identification of when one subject is completed
10 and the other begins.

11 Q. What is the linking sequence?

12 A. So to be most precise, in the paragraph
13 that I just quoted from it's referencing a figure
14 in the Travers '75's specification, which is
15 Figure 2A. Figure 2A includes a number of
16 numerical annotations to describe different
17 components of the molecule, and the linking
18 sequence corresponds to the numerical annotation
19 206.

20 Q. Does linker sequence 206 include a
21 noncomplementary portion?

22 ATTORNEY POWERS: Object to form.

23 A. Can you please define what you mean by
24 "noncomplementary portion"?

25 Q. Do you know what complementary means in

1 the context of nucleotides?

2 A. Yes, I do.

3 Q. Okay. Does 206 include a sequence of
4 nucleotides that are noncomplementary to each
5 other?

6 A. I don't think the question is correctly
7 posed, I apologize. 206 includes a series of
8 nucleotides. Some of them -- this is a single-
9 stranded molecule. Some of those nucleotides may
10 be complementary to each other; some of them may
11 not be.

12 I don't know precisely what you mean by
13 your question.

14 Q. You used the term "single-stranded."
15 Does 206 include a single-stranded region?

16 A. Yes, in Figure 2A, 206 is depicted as a
17 single-stranded linker sequence.

18 Q. Can you turn to paragraph 141 of your
19 declaration and let me know when you're there.

20 A. Okay.

21 Q. The first sentence you indicate that
22 the circular template of Travers contains a single
23 primer polymerase binding site. Do you see that?

24 A. I do see that.

25 Q. The primer binding site is located in

1 the adapter portion of the circular template; is
2 that correct?

3 A. Yes, that's correct.

4 Q. Does Travers illustrate adapters on
5 each end of a DNA fragment?

6 A. Yes, it does.

7 Q. If there is only one primer binding
8 site but adapters on each end, does that mean that
9 there are different adapters on each end of the
10 fragment?

11 A. It can mean that.

12 Q. If one adapter has a primer binding
13 site and the other doesn't, they are nonidentical
14 in at least that capacity; correct?

15 A. That is correct.

16 Q. Let's turn to paragraph 102 of your
17 declaration. Let me know when you're there.

18 A. Okay. I'm there.

19 Q. A few sentences into this paragraph you
20 state, Schadt 2010 taught, quote, SMRT sequencing
21 does not require routine PCR amplification needed
22 by most SGS systems, thereby avoiding systematic
23 amplification bias, end quote.

24 Do you see that?

25 A. I do see that.

1 Q. Is rolling circle replication
2 considered routine PCR amplification?

3 A. Sorry, I apologize. I'd like to go
4 back and modify a previous answer.

5 Q. Let's answer the question.

6 A. I'll answer this question, and then I'd
7 like to go back and modify.

8 Q. Let's answer the question, and then
9 we'll figure out what we're going to do.

10 A. Okay.

11 Q. Let me re-pose the question.
12 Is rolling circle replication
13 considered routine PCR amplification?

14 A. Rolling circle replication is not
15 considered routine PCR amplification. Okay.

16 Q. Hold on.

17 ATTORNEY POWERS: If you want to say
18 something, Doctor, please do.

19 A. What I would like to modify is you had
20 previously asked if in Travers '75 the two adapter
21 molecules on the different ends of the molecule
22 were the same or if they were different. And I
23 wanted to highlight that it's possible for them to
24 be the same adapter sequence molecule.

25 Q. Okay. Thank you.

1 All right. Let's turn to page 108 of
2 your declaration. Let me know when you're there.

3 A. Okay. I'm there.

4 Q. I need some help in interpreting this
5 figure.

6 A. Sure.

7 Q. Let's start with the SMRTbell that's
8 illustrated on the right side. So what is this
9 molecule? I can ask you more specifically.

10 Does this correspond to the molecule
11 that's labeled circular product and hairpin
12 ligation that's shown on page 103?

13 A. So on page 103 I depict the circular
14 product that is described in Travers that would
15 occur after performing hairpin ligation but prior
16 to any potential amplification steps. And that is
17 the molecule that I am depicting on the right of
18 the figure on page 108.

19 Q. And this is a molecule with 168 base
20 pair long insert; is that correct?

21 (Pause.)

22 A. I'm hoping I list the size of the
23 insert in my report so I don't have to count.

24 Q. Let me help you out.

25 A. Thank you.

1 Q. Footnote 11 mentions 168 base pair long
2 insert.

3 A. Thank you.

4 Q. And page 102 at the top mentions 149
5 base pair insert.

6 A. Right. Thank you.

7 Q. So it's clear what's being illustrated,
8 that 149 base pair insert was used to create this
9 circular product on page 103; correct?

10 A. Yeah, that's correct.

11 Q. And that circular product on page 103
12 is illustrated on the right side of the page 108
13 figure labeled SMRTbell circular sequencing;
14 correct?

15 A. That's correct.

16 Q. Okay. Thank you.

17 So back to the figure on page 108.

18 This figure is indicating that the SMRTbell with
19 the 149 base pair insert is about 50 nanometers
20 long; is that correct?

21 ATTORNEY POWERS: Object to form.

22 A. Could you repeat the question, sorry?

23 Q. The right side of the figure on page
24 108 is indicating that the SMRTbell is about 50
25 nanometers long; correct?

1 A. That's correct.

2 Q. And, again, the SMRTbell is a SMRTbell
3 with 149 base pair insert?

4 ATTORNEY POWERS: Object to form.

5 A. That's correct.

6 Q. And this green check mark that you have
7 indicates that you think this SMRTbell would fit
8 in the ZMW well; is that correct?

9 A. That's correct.

10 Q. I think you say this in your
11 declaration, but the SMRTbell that's shown in the
12 figure here on page 108 is a two-dimensional
13 schematic; correct?

14 A. That's correct.

15 Q. But DNA in solution doesn't assume a
16 rigid conformation like a piece of lumber;
17 correct?

18 A. That's correct.

19 Q. I credit you for acknowledging this. I
20 believe at 107 and again I believe later, just to
21 be clear. Sorry, you don't have to -- paragraph
22 188 you acknowledge that the precise three-
23 dimensional structure of the folded concatemer
24 molecule will also fluctuate in solution; correct?

25 A. In paragraph 188 I say, A person of

1 ordinary skill in the art would understand that
2 the precise three-dimensional structure of the
3 folded concatemer molecule would also fluctuate in
4 solution.

5 Q. Okay. Let's look at the concatemers on
6 the left side of the figure on page 108. Let me
7 hand you a couple of exhibits. The first is
8 Exhibit 2069.

9 I'm also handing you a copy of Exhibit
10 2070 and, finally, a copy of Exhibit 2071. Do you
11 recognize these exhibits?

12 A. I do.

13 Q. And these exhibits were submitted with
14 your declaration; correct?

15 A. Yes, that's correct.

16 Q. So turning back to the figure at page
17 108, let's first look at the concatemer to the far
18 left. Let me know when you're there.

19 A. Okay.

20 Q. Is this the same molecule shown in
21 Exhibit 2069?

22 ATTORNEY POWERS: Object to form.

23 (Pause.)

24 A. The figure on page 108 does not show a
25 specific molecule or sequence, whereas Exhibit

1 2069, while the letters are admittedly small, does
2 refer to a specific molecular sequence. I'm
3 attempting to visualize the overall structure of
4 that sequence in the figure on page 108.

5 Q. Okay. Understood.

6 My question is very simple. I'm just
7 trying to draw a comparison to identify what's
8 what.

9 With that in mind, is the concatemer on
10 the far left of the figure on page 108
11 corresponding to what's shown in Exhibit 2069?

12 A. So, as I say in my report -- my
13 declaration, excuse me, in paragraph 189, the
14 left-most panel corresponds to a structure formed
15 after three full loops, which is also the
16 structure that I am showing in Exhibit 2069.

17 Q. Okay. Exhibit 2069 at the bottom
18 identifies this molecule as having 1008 base
19 pairs. Do you see that?

20 A. I see those numbers, 1008 base pairs,
21 or BP.

22 Q. BP.

23 A. Yeah.

24 Q. Right.

25 So my question is should this be 1008

1 nucleotides rather than base pairs.

2 A. So that -- excuse me. Let me take a
3 second.

4 So Exhibit 2069 shows the output of a
5 secondary structure prediction tool that I used.
6 When I -- as you can see from my declaration, I
7 submitted multiple different analyses that
8 corresponded to different numbers of loops. The
9 name -- every time that I submitted an analysis,
10 it asked me to put in a unique name. In this case
11 I used the name to denote to myself which
12 structure that I was putting in.

13 The number of nucleotides or base pairs
14 that's present in the end is not guaranteed to be
15 an accurate reflection of the total -- that's
16 not -- I wasn't trying to make a statement there.
17 That's just a number that I used for myself.

18 What the title of this molecule is
19 meant to denote here is that this is a structure
20 that would occur if there were six -- let me just
21 speak precisely.

22 If the rolling circle replication
23 process generated a concatemer comprising 6X
24 copies of the original insert, which is three full
25 loops through the circle.

1 So I wouldn't say that the title should
2 or should not be anything.

3 Q. Trust me, I'm not going to criticize
4 you for the title.

5 A. Okay.

6 Q. I'm just trying to understand the
7 number of nucleotides that are present in the
8 molecule. I really appreciate the clarification.

9 So with that in mind, is it correct to
10 say that there are 1008 nucleotides in this
11 molecule?

12 A. 1008 I believe is 168 times 6. I
13 believe that is correct. I will withhold the
14 counting.

15 Q. You want me to just tell you how I came
16 to the number and we'll start there?

17 A. Uh-huh.

18 Q. It looked like the circular product
19 after hairpin ligation molecule shown on page 103
20 came to 336 nucleotides.

21 A. Uh-huh.

22 Q. And 336 times 3 is 1008.

23 A. Yes. Or 168 times 6. Anyway, yes,
24 I...

25 Q. We have to account for the nucleotides

1 in the linker molecules.

2 A. I agree that the 336 times 3 is 1008,
3 and I believe that reflects the number of
4 nucleotides present in Exhibit 2069.

5 Q. Great.

6 I'm going to ask you similar questions
7 for the next two concatemers. Okay? Turn back to
8 the figure at page 108. Let me know when you're
9 there.

10 A. Okay.

11 Q. Does the concatemer in the middle of
12 the left panel correspond to the molecule shown in
13 Exhibit 2070?

14 A. So the molecule shown in the middle of
15 Figure 108 is meant to be a visual representation
16 of the secondary structure that would be formed by
17 a concatemer comprising ten copies or five full
18 circles that originated from the rolling circle
19 replication process, which is what is shown in
20 Exhibit 2070.

21 Q. Thank you.

22 And 2070 recites 1680 BP; correct?

23 A. That's the name on the title of the
24 exhibit.

25 Q. Right.

1 As far as the number of nucleotides, is
2 it accurate to read this as having 1680
3 nucleotides?

4 A. Yes, that is accurate.

5 Q. Okay. Thank you.

6 Let's turn back to the figure on page
7 108, and we'll do this one more time. Let me know
8 when you're there.

9 A. I'm there.

10 Q. The concatemer on the right side of the
11 left panel, does that correspond to the molecule
12 shown in Exhibit 2071?

13 A. So the molecule depicted on the right
14 side of the left panel is meant to schematicize
15 the secondary structure formed by the concatemer
16 that would be generated by a rolling circle
17 replication process that generated ten circles,
18 which is also the specific molecule depicted in
19 Exhibit 2071.

20 Q. Thank you.

21 And Exhibit 2071 at the bottom recites
22 3360 BP in the title; is that correct?

23 A. That's the word listed there.

24 Q. And am I correct in understanding that
25 the molecule has 3,360 nucleotides?

1 A. I believe so, yes.

2 Q. Thank you.

3 ATTORNEY POWERS: Mike, we've been
4 going more than an hour. Is now a good time?

5 ATTORNEY ROSATO: Let's take a break.

6 (Recess taken from 1:56 to 2:01.)

7 Q. Dr. Satija, during the break did you
8 have any discussions with counsel?

9 A. Nothing related to my testimony today.

10 Q. During any of the breaks did you
11 discuss your testimony with counsel?

12 A. No.

13 Q. Appreciate that. We expect nothing
14 less.

15 Let's hand you a copy of Exhibit 2007.
16 Do you recognize this reference?

17 A. I'll take a moment to read it, please.
18 (Pause.)

19 A. Yes, I recognize this.

20 Q. Do you recognize it as the Kirsch
21 reference that's discussed at paragraph 227 of
22 your declaration?

23 A. That's correct.

24 Q. Can you look at Figure 1 of Kirsch,
25 please. Let me know when you're there.

1 A. Okay.

2 Q. What is depicted in Figure 1 of Kirsch?

3 A. So Figure 1 of Kirsch is titled and
4 what it depicts is the process of sequence error
5 correction by different methods.

6 Q. What methods are depicted in Figure 1?

7 A. So to be precise I'll read from the
8 Figure 1 legend. On the left are depicted
9 standard methods for the correction of sequencing
10 errors which use the abundance of a sequence read
11 to identify errors.

12 In the middle is depicted SSCS, or
13 analogous to the Kirsch claim Safe-Seq, which use
14 identifiers on single-strand molecules to group
15 families of sequence reads and remove those that
16 occur less frequently than in 95 percent of family
17 reads.

18 And on the right is depicted duplex
19 sequencing, which, in addition to assigning
20 families of single strand reads, exploits the
21 information from the complementary strand.

22 Q. I heard you mention three different
23 methods; is that correct?

24 A. That's correct.

25 Q. And those are depicted as standard NGS

1 technology as one; is that correct?

2 A. That's the title of the box in Figure 1
3 depicting standard methods for the correction of
4 sequencing errors that use the abundance of a
5 sequence read to identify errors.

6 Q. And the title of the second box is
7 SSCS/Safe-SeqS; correct?

8 A. That's correct.

9 Q. And the third box is DCS; correct?

10 A. That's the title, yes.

11 Q. And DCS stands for duplex consensus
12 sequencing; is that correct?

13 A. Yes, that's correct. The acronym is
14 spelled out in the second column of page 1.
15 However, it also identifies the complementary DNA
16 strand by searching for the complementary tag
17 sequence among the SSCS duplex consensus
18 sequences, DCS.

19 Q. Thank you.

20 You mentioned the middle column of the
21 first page previously; is that correct? There's
22 three columns here?

23 A. There is a middle column, yes.

24 Q. In the middle column of the first page,
25 Kirsch cites to a recently published approach term

1 Safe-Seq. Do you see that?

2 A. If you were reading from the article,
3 can you tell me exactly where?

4 Q. Middle column, first few lines.

5 A. I see it.

6 Q. And the citation is to reference number
7 6. Do you see that?

8 A. I do see that.

9 Q. And what is reference number 6?

10 A. Reference number 6 is an article that
11 appears in the journal proceedings of the National
12 Academy of Sciences in 2011. The first author is
13 Kinde.

14 Q. Who are the other authors on that
15 paper?

16 A. Wu, Papadopoulos, Kinzler, and
17 Vogelstein.

18 Q. Are you familiar with this Kinde
19 reference?

20 A. I am, yes.

21 Q. Okay. Let's hand you a copy of that.
22 It's Exhibit 1006 in this proceeding.

23 A. I'm just going to take a moment to
24 refresh my memory.

25 (Pause.)

1 A. Okay. Thank you.

2 Q. You mentioned you're familiar with the
3 Kinde reference; correct?

4 A. I believe I cite it as an exhibit in my
5 report.

6 Q. That's listed on page 10 of your
7 declaration; right?

8 A. Yes, I see it there.

9 Q. Turning back to Kirsch, how is Kirsch
10 distinguishing in Figure 1 between Safe-Seq/SSCS
11 on the one hand and DCS on the other?

12 ATTORNEY POWERS: Object to form.

13 A. So Kirsch in this figure depicts at the
14 beginning of the figure a DNA molecule with a TRIM
15 mutation. In the subsequent steps Kirsch
16 demonstrates a variety of artifacts that can occur
17 to the DNA molecule during the sample preparation
18 process.

19 For example, in the second box an error
20 is introduced into the DNA molecule by deamination
21 or oxidative stress. And then in the boxes below,
22 additional artifacts are introduced into the
23 molecule during a subsequent amplification step,
24 which in this case is schematicized by PCR.

25 Kirsch then demonstrates -- attempts to

1 visually demonstrate how the different methods
2 would deal with this type of -- each type of
3 artifact and at the bottom of each box depicts the
4 final output of the DNA sequencing process.

5 So, for example, in the DCS box on the
6 right, there is only a single mutation that occurs
7 after error correction by DCS. And that single
8 mutation, which is schematicized with the blue
9 circle, corresponds to the true mutation that was
10 introduced in the first box.

11 One of the differences that Kirsch
12 notes between DCS and Safe-Seq is that in Safe-Seq
13 additional mutations will continue to be detected
14 in the molecule despite the fact that those were
15 not originally true mutations that were present
16 in vivo.

17 Q. Let me ask you about that. So when
18 you're talking about the mutations, are you
19 talking about in the Safe-Seq box the lower two --
20 the strands at the lower -- the most -- the
21 bottommost portion of that box?

22 A. Correct. So, for example, in the
23 bottommost portion of the box, which occurs after
24 error correction by Safe-Seq, the molecules
25 include a blue X and a blue diamond. And if we

1 look at the legend in Figure 1, we can see that
2 those annotations correspond to artifacts
3 introduced either by spontaneous deamination or,
4 for example, oxidative stress.

5 In contrast, the bottom strands of the
6 DCS do not include these annotations because they
7 have been removed by the DCS error correction
8 procedure. So that's a difference that Kirsch
9 draws between the Safe-Seq procedure and DCS.

10 Q. When you're referring to the bottom
11 strands in DCS, are you referring to the strands
12 that are labeled with complementary tag alignment
13 and error correction by DCS?

14 A. I am referring to strands that occur
15 after error correction by DCS. As I mentioned in
16 Figure 1, the purpose of this figure, as is clear
17 from the title, is to demonstrate sequence error
18 correction by different methods.

19 And so what this figure is trying to
20 schematicize is the final output of these three
21 procedures after performing the error correction
22 steps that are taught by each method. And the
23 conclusion from the figure is that only in the DCS
24 method are the true biological mutations recovered
25 but the artifactual mutation, either from PCR

1 sequencing artifacts or from deamination and
2 oxidative stress, were removed.

3 Q. Okay. So both methods are looking at
4 error correction; correct?

5 ATTORNEY POWERS: Object to form.

6 A. So the word "error correction" appears
7 in all three boxes, but the type of error
8 correction is different between the methods.

9 Q. I think what you indicated there was
10 Kirsch is indicating that error correction was
11 more effective in DCS compared to prior methods?

12 A. So Kirsch is indicating a number of
13 things in this figure. In the final output -- you
14 had asked me one way in which they differentiate
15 between Safe-Seq and DCS. One key differentiating
16 fact is the output of the procedure, which is a
17 lack of artifacts that are present in the DCS
18 output but are detected artifactual mutations that
19 were not originally present in vivo when using
20 Safe-Seq.

21 Kirsch also depicts that there are
22 differences in the error correction procedure
23 between the methods which in fact enable the
24 superior result and in fact relate to the claims
25 of the '127 patent, which is I why I discuss it in

1 my report.

2 Q. What differences in the error
3 correction procedure does Kirsch identify?

4 A. So as I say in my declaration, for
5 example, in paragraph 231, Dr. Kirsch states that
6 the duplex sequencing method involves identifying
7 families of DNA molecules that share the same tag
8 on a single strand and then, in addition,
9 identifying the, quote, complementary DNA strand
10 by searching for the complementary tag sequences.
11 That is a unique feature of the DCS technology and
12 not the Safe-Seq technology.

13 Q. Can you turn to page 3 of the
14 supplement in the Kinde paper. Let me know when
15 you're there, please.

16 A. I'm there. I'd just like a minute to
17 read through it, please. This is page 3, you
18 said?

19 Q. Page 3 of the supplement.

20 A. Supplement.

21 Q. Yeah.

22 (Pause.)

23 A. Okay. Thank you. I'm here.

24 Q. Could you see the sentence in the
25 middle, the second paragraph on the left -- in the

1 left column on page 3 that reads, When requiring
2 multiple super mutants, the specificity can be
3 further increased by requiring that each strand of
4 the original double-stranded template contain the
5 mutation?

6 A. I can see that sentence. But I feel
7 that in order to interpret that sentence it's
8 important to read the Kinde specification as a
9 whole.

10 Q. Sure.

11 So back to paragraph 231 of your
12 declaration, you pointed me to the second sentence
13 where you state, Dr. Kirsch states that the duplex
14 sequencing method involves identifying families of
15 DNA molecules that share the same tag sequence on
16 a single strand and then identifying complementary
17 DNA strand by searching for the complementary tag
18 sequences.

19 Do you see that?

20 A. I do see that.

21 Q. So there's two components there. I
22 want to ask about them in turn, starting with the
23 first one, families of DNA molecules that share
24 the same tag sequence on a single strand. Okay?

25 A. Okay. Already.

1 Q. Is it your understanding that Kinde
2 does not disclose identifying families of DNA
3 molecules that share the same tag sequence on a
4 single strand?

5 ATTORNEY POWERS: Object to form.

6 A. That's not my precise understanding.

7 Q. Okay. Let me ask you about the second
8 component, that is, identifying the complementary
9 DNA strand by searching for the complementary tag
10 sequence. Okay?

11 A. Okay.

12 Q. Is it your understanding that Kinde
13 does not disclose identifying the complementary
14 DNA strand by searching for the complementary tag
15 sequences?

16 ATTORNEY POWERS: Objection, form,
17 scope.

18 A. It is it is not my understanding that
19 Kinde teaches identifying the complementary DNA
20 strand by searching for complementary tag
21 sequences.

22 Q. Just a moment ago we read from page 3
23 of Kinde; right?

24 A. Uh-huh.

25 Q. And we read a statement in Kinde that

1 says, When requiring multiple super mutants the
2 specificity can be further increased by requiring
3 that each strand of the original double-stranded
4 template contain a mutation.

5 Do you remember reading that?

6 A. I do. I also said that I felt that in
7 order to interpret that statement accurately it
8 was necessary to read the Kinde specification as a
9 whole.

10 Q. Understood.

11 So my question is does that disclosure
12 not amount to identifying the complementary DNA
13 strand by searching for the complementary tag
14 sequences.

15 A. It does not.

16 ATTORNEY POWERS: Objection to form.

17 Q. What's your basis for saying it
18 doesn't?

19 A. So I realize also that this is not a
20 topic that I offer an opinion on in my report, but
21 I'm answering questions about it. But I want to
22 highlight that this is not an issue that I offer
23 an opinion on in my report, but I'm interpreting
24 the reference with you here today.

25 So the Kinde reference does not teach

1 the use of barcodes to link reads to either the
2 first strand or the second strand. That teaching
3 is not present in Kinde.

4 This is highlighted also, as we
5 discussed, by Kirsch, which highlights the unique
6 aspect of duplex consensus sequencing, which is
7 the ability to link a molecule to a particular
8 strand. That feature is only present in duplex
9 consensus sequencing and not in Safe-Seq.

10 To respond more specifically to your
11 question, I believe a person of ordinary skill in
12 the art would not simply read the sentence that
13 you had asked me about but would read, for
14 example, the surrounding paragraphs as part of the
15 overall context.

16 If I look at page 2 of the
17 supplementary material, I'm in the second
18 paragraph from the end. I'll start a couple of
19 sentences in.

20 The errors from error-generating
21 process 8 can be reduced by requiring at least two
22 super mutants to identify a position as a mutant.
23 This requirement is reasonable because every
24 preexisting mutation in a double-stranded DNA
25 template should give rise to two super mutants,

1 one from each strand.

2 So the language here is crystal clear.
3 Kinde is not actually searching for complementary
4 sequences to be able to determine conclusively
5 first and second strand identity. What Kinde is
6 doing instead is simply looking for two super
7 mutants, which could have originated from
8 different molecules, and saying that that is a
9 reasonable proxy for being able to assume that a
10 mutation must exist on two strands.

11 But the language is clear that it is
12 not actually teaching a method to link an
13 individual DNA sequence read to a first or second
14 strand. That is not taught in Kinde.

15 Q. Where does it say reasonable proxy?

16 A. So it says, This requirement is
17 reasonable because every preexisting mutation in a
18 double-stranded DNA template should give rise to
19 two super mutants, one from each strand.

20 Q. I see how it says that. What I don't
21 see is how it's saying this whole other thing is a
22 reasonable proxy for something else. Where is
23 that stated?

24 A. So these two sentences next to each
25 other, one is that the errors from error-

1 generating processes can be reduced by requiring
2 at least two super mutants to identify a position
3 as mutant, followed by the sentence that this
4 requirement is reasonable because every
5 preexisting mutation in a double-stranded DNA
6 template should give rise to two super mutants,
7 one from each strand.

8 Those are different things. The goal
9 of being able to identify a preexisting mutation
10 that occurs in two molecules, which is what
11 they're saying in the first sentence, is different
12 than the goal of being able to identify a mutation
13 that exists on two strands of the same molecule.

14 But here Kinde is tying these two
15 statements together. They say that this
16 requirement -- this is in the second sentence --
17 sorry, that the requirement described in the first
18 sentence is justified by the second sentence.

19 And what I'm saying is a person of
20 ordinary skill in the art would realize when
21 reading the Kinde specification that Kinde is not
22 teaching the process that's described in duplex
23 consensus sequencing or as described by Kirsch.

24 Q. Your comment about reasonable proxy
25 that was your interpretation, that's not indicated

1 in Kinde?

2 A. So what's stated in Kinde is the words
3 "this requirement," which is --

4 Q. Two super mutants is the requirement.

5 ATTORNEY POWERS: Please don't
6 interrupt the witness, counsel.

7 A. I'll start again.

8 What's stated in Kinde is that this
9 requirement, which relates to a previous sentence
10 regarding the need for two super mutants, which
11 could exist on completely different molecules,
12 that requirement is reasonable because every
13 preexisting mutation should be present on both
14 strands.

15 Those are two very different things.
16 One -- a person of ordinary skill in the art would
17 recognize that one does not necessarily justify
18 the other. So a person of ordinary skill in the
19 art would recognize that Kinde is not teaching a
20 method to link individual sequence reads to either
21 first or second strands, as is very clearly done
22 by duplex sequencing technology.

23 Q. Back to paragraph 231, because I want
24 to make sure that we're talking about the same
25 thing, paragraph 231 we were talking about your

1 statement that says, Identifying the complementary
2 DNA strand by searching for the complementary tag
3 sequence; right?

4 A. That's the process that's performed in
5 duplex sequencing. That's what I was referring
6 to.

7 Q. This is what I want to clarify. Do you
8 dispute that Kinde discusses distinguishing
9 between mutations in one strand versus the other?

10 ATTORNEY POWERS: Objection to form,
11 foundation, scope.

12 A. So I don't form or I don't offer an
13 opinion to this specifically in my declaration.

14 Q. That's not actually true. You're
15 citing to Kirsch as objective indicia; right? And
16 you are citing at Kinde on page 10 as a document
17 you considered.

18 Am I wrong about that?

19 A. Can you repeat the previous question?
20 Sorry.

21 Q. You said you didn't offer an opinion,
22 but you did discuss Kirsch in your declaration;
23 correct?

24 A. I do discuss Dr. Kirsch in my
25 declaration.

1 Q. And you cite specifically to the Kinde
2 reference in your declaration; correct?

3 ATTORNEY POWERS: Objection.

4 A. I know I list the Kinde reference in my
5 list of exhibits. I don't know if I cite
6 specifically to it.

7 Q. Well, okay. Do persons of ordinary
8 skill read papers and not critically analyze the
9 content that's being discussed?

10 A. You asked me if I cited Kinde in my
11 declaration. That's the question that I was
12 responding to.

13 Q. And my pushback was in regard to your
14 statement that you didn't consider this stuff in
15 your declaration --

16 ATTORNEY POWERS: Objection to form.

17 Q. -- which isn't true.

18 ATTORNEY POWERS: Objection to form,
19 argumentative.

20 A. I think it's accurate to say that in my
21 declaration I don't offer a specific opinion on
22 Kinde.

23 Q. Okay. I'm going to ask specific
24 questions about Kinde, because it is cited in your
25 declaration.

1 A. Okay.

2 Q. And it's also the entire basis of the
3 comparison of the Kirsch document. Okay?

4 A. Okay.

5 Q. When Kinde discusses requiring that
6 each strand of the original double-stranded
7 template contain a mutation, doesn't that suggest
8 that Kinde's considering both strands of the
9 template?

10 ATTORNEY POWERS: Objection, asked and
11 answered, form.

12 A. I disagree with the statement that
13 Kinde teaches a method to be able to assign reads
14 to either the first or second strand.

15 I'll elaborate. While -- no, I've
16 finished my answer.

17 Q. So just turning back to Kirsch, you
18 previously talked about the first few lines of the
19 middle column where it cites to Kinde; correct?

20 A. That's correct.

21 Q. The next sentence states, However, it
22 also identifies the complementary DNA strand by
23 searching for the complementary tag sequences
24 among the SCS reads duplex consensus sequencing,
25 DCS; correct?

1 A. Those are the words in the Kirsch
2 reference.

3 Q. By "it," it's referring to the Schmitt
4 paper, not Kinde; correct?

5 A. It refers to this approach that is
6 practiced by the Schmitt paper, which is referred
7 to as duplex consensus sequencing, which is also
8 the title of the '127 patent.

9 Q. Okay. Great.

10 A. Or in the summary of the '127 patent.

11 Q. Okay. Previously you said you disagree
12 with the statement that Kinde teaches a method to
13 assign reads to either the first or second strand;
14 correct?

15 A. That's correct.

16 Q. Does Kirsch say that there's no such
17 distinction in Kinde?

18 ATTORNEY POWERS: Objection to form.

19 A. Kirsch is very clear that the duplex
20 consensus sequencing method represents an advance
21 over existing methods, and it highlights that that
22 specific advance, in the paragraph -- in the
23 sentence that we just covered, is that when
24 performing duplex consensus sequencing it also
25 identifies the complementary DNA strand by

1 searching for the complementary tag sequence.

2 So that is a distinguishing factor that
3 is unique to the duplex consensus sequencing
4 method. And the uniqueness of this is supported
5 not only by how a person of ordinary skill in the
6 art would read the reference, as Dr. Kirsch did,
7 but by the text in the Kirsch reference and also
8 by Figure 1 in the Kirsch reference.

9 Q. Would a person of ordinary skill read a
10 reference by deleting content when they quote
11 sentences?

12 ATTORNEY POWERS: Objection, form,
13 foundation, misleading.

14 A. I believe it's important to understand
15 the content or to understand a sentence in its
16 proper context, but I don't agree with the
17 statement that by definition removing a word would
18 be inappropriate for a person of ordinary skill in
19 the art to do, especially when trying to summarize
20 an article, as Dr. Kirsch is doing so here.

21 Q. Okay. I ask because when you quoted
22 this sentence in the middle column of Kirsch you
23 left out the key part, and that is searching for
24 the complementary tag sequences among the SSCS
25 reads. You omitted reference to the SSCS reads.

1 Was that accidental?

2 ATTORNEY POWERS: Objection to form.

3 A. I don't believe that my statement
4 mischaracterizes the Kirsch reference or
5 mischaracterizes the capabilities of duplex
6 consensus sequencing.

7 Q. Okay. But just to be clear on what's
8 stated in Kirsch, the sentence we're talking about
9 states, However, it also identifies the
10 complementary DNA strand by searching form the
11 complementary tag sequences among the SSCS reads,
12 duplex consensus sequences, DCS; correct?

13 A. Those are the words in the Kirsch
14 reference.

15 Q. Okay.

16 I'm going to hand you a copy of Exhibit
17 1022. Do you recognize this reference?

18 (Pause.)

19 A. I do see that it's listed as an exhibit
20 to my report; is that correct? It's listed as
21 Exhibit 1022. I don't immediately recall all the
22 details of this reference.

23 Q. Okay. This is the Vogelstein PCT,
24 which corresponded to the Kinde reference.
25 Vogelstein is an author on the Kinde reference.

1 And it's submitted as Exhibit 1022 and cited at
2 page 12 of your declaration, if you want to go
3 check that. Okay?

4 A. Okay.

5 Q. Previously you stated, I disagree with
6 the statement that Kinde teaches a method to be
7 able to assign reads to either the first or second
8 strand. Do you remember that?

9 A. I do.

10 Q. Can you turn to paragraph 42 of
11 Vogelstein?

12 ATTORNEY POWERS: Objection, scope.

13 Q. So a few lines down in paragraph 42
14 Vogelstein states, The two strands of the double-
15 stranded template can be differentiated by the
16 observed orientation of the sequences and the
17 order in which they appear when sequence
18 information is obtained from both ends.

19 Do you see that?

20 A. I'm sorry, can you start again? I
21 missed where you were starting from. This is page
22 42?

23 Q. Paragraph 42.

24 A. Oh, paragraph 42. Give me a second.
25 (Pause.)

1 A. Okay.

2 Q. Okay. A few lines down in paragraph 42
3 there is the sentence the two strands of the
4 double-stranded template can be differentiated by
5 the observed orientation of the sequences and the
6 order in which they appear when sequence
7 information is obtained from both ends.

8 Do you see that?

9 A. I do see that statement.

10 Q. The last sentence of paragraph 42
11 states, Requiring that mutations occur in only one
12 or in both strands so the templates can further
13 increase the specificity of Safe-SeqS.

14 Do you see that?

15 A. So I can see the sentences that you're
16 giving to me, and I do say that I reviewed this
17 document in preparing my declaration.

18 But I think you're asking me about
19 something that goes beyond the scope of the
20 testimony that I've given in my declaration and
21 that I haven't offered a specific opinion on in my
22 declaration.

23 So this is a long patent document, and
24 it's not something that I offered an opinion on or
25 that I was asked to offer an opinion on or that I

1 believe even Dr. Quackenbush offers an opinion on
2 in this case. So -- at least in this particular
3 IPR.

4 So I can see the sentences that you're
5 presenting to me, but I really feel that this
6 is -- sitting here today these are long documents,
7 and I'm unable to remember the entire context,
8 having not offered an opinion on this topic
9 before.

10 Q. Okay. Well, let's just finish out the
11 questions I have on this paragraph.

12 A. I'm happy to agree that the words on
13 the page are the words that you're reading, but I
14 can't offer specific opinions or interpretations
15 on them today without an opportunity to look
16 through this over time.

17 Q. Are you able to confirm that this
18 paragraph is discussing paired-end sequencing?

19 ATTORNEY POWERS: Objection, scope.

20 A. I can confirm the specific words that
21 are on the page, but I cannot confirm that this
22 paragraph is discussing paired-end sequencing as a
23 person of ordinary skill in the art would use the
24 term.

25 Q. So three sentences down paragraph 42

1 states, This type of sequencing experiment is
2 called a paired-end run on the Illumina platform,
3 but similar experiments can be done on other
4 sequencing platforms where they may be called by
5 another name.

6 Do you see that?

7 A. I can --

8 ATTORNEY POWERS: Objection, scope.

9 Go ahead.

10 A. I can see those words on the page. I
11 would just highlight because the words "paired
12 end" are used doesn't necessarily mean that the
13 application teaches an embodiment that uses
14 paired-end sequencing.

15 This is not something that I've formed
16 an opinion on as part of this case, and I would
17 need to review the specification in detail over
18 time in order to be able to answer that question.

19 Q. Okay. Do you think this disclosure in
20 Vogelstein would be relevant to your earlier
21 statement where you said, I disagree with the
22 statement that Kinde teaches a method to be able
23 to assign reads to either the first or second
24 strand?

25 ATTORNEY POWERS: Objection, scope.

1 A. So you had asked me a very specific
2 question about a Kinde reference that was cited
3 specifically by the Kirsch commentary. My
4 statement was related to that reference and in
5 that context.

6 ATTORNEY ROSATO: Let's take a break.

7 (Recess taken from 2:58 to 2:59.)

8 Q. Let's turn back to the '127 patent,
9 please. Front page of the '127 patent lists three
10 inventors; is that correct?

11 A. I see three names listed there: Jesse
12 Salk, Lawrence Loeb, and Michael Schmitt.

13 Q. And do you know any of these
14 individuals?

15 A. I do not.

16 Q. You don't know anything about their
17 background or reputation?

18 A. I've heard of these individuals before,
19 and I've heard people speak of them in a positive
20 context. But I don't know them personally.

21 Q. Do you know if they're viewed in the
22 scientific community as credible scientists?

23 A. I certainly believe so, yes.

24 Q. And at your declaration paragraphs 28
25 through 30 you discuss a person of ordinary skill

1 in the art; correct?

2 A. Yes, that's right.

3 Q. Do you have any reason to believe that
4 any of these inventors would fail to meet that
5 description of a person of ordinary skill in the
6 art?

7 ATTORNEY POWERS: Objection, scope.

8 A. I have no reason to believe that.

9 ATTORNEY ROSATO: Thank you. No
10 further questions.

11 THE WITNESS: Thank you.

12 ATTORNEY POWERS: No questions here.

13 (Time noted: 3:00 p.m.)

14 _____

15 RAHUL SATIJA

16

17 Subscribed and sworn to before me

18 this ____ day of _____ 2023.

19

20 _____

21

22

23

24

25

C E R T I F I C A T E

STATE OF NEW YORK)

: ss.

COUNTY OF NEW YORK)

I, LAURIE A. COLLINS, a Registered
Professional Reporter and Notary Public
within and for the State of New York, do
hereby certify:

That RAHUL SATIJA, the witness whose
deposition is hereinbefore set forth, was
duly sworn by me and that such deposition
is a true record of the testimony given by
the witness.

I further certify that I am not
related to any of the parties to this
action by blood or marriage and that I am
in no way interested in the outcome of this
matter.

IN WITNESS WHEREOF, I have hereunto
set my hand this 31st day of March 2023.



LAURIE A. COLLINS, RPR

1 - - - - - I N D E X - - - - -

2

3 WITNESS: EXAMINATION BY: PAGE

4 Rahul Satija Attorney Rosato 3

5

6 ----- EXHIBITS -----

7 NO. DESCRIPTION PAGE

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9 - none -

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CASE: Guardant Health v. University of Washington

DEPOSITION DATE: March 21, 2023

DEPONENT: Rahul Satija

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RAHUL SATIJA
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write 92:2	zmw 120:8
written 32:23	
38:24	
wrong 61:20	
143:18	
wsgr.com 2:18	
2:20	
wu 130:16	

Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

DISCLAIMER: THE FOREGOING FEDERAL PROCEDURE RULES ARE PROVIDED FOR INFORMATIONAL PURPOSES ONLY.

THE ABOVE RULES ARE CURRENT AS OF APRIL 1, 2019. PLEASE REFER TO THE APPLICABLE FEDERAL RULES OF CIVIL PROCEDURE FOR UP-TO-DATE INFORMATION.

VERITEXT LEGAL SOLUTIONS
COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

Veritext Legal Solutions is committed to maintaining the confidentiality of client and witness information, in accordance with the regulations promulgated under the Health Insurance Portability and Accountability Act (HIPAA), as amended with respect to protected health information and the Gramm-Leach-Bliley Act, as amended, with respect to Personally Identifiable Information (PII). Physical transcripts and exhibits are managed under strict facility and personnel access controls. Electronic files of documents are stored in encrypted form and are transmitted in an encrypted fashion to authenticated parties who are permitted to access the material. Our data is hosted in a Tier 4 SSAE 16 certified facility.

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