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UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

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INTEGRATED DNA TECHNOLOGIES, INC.,

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Petitioner,

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V.

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TECAN GENOMICS, INC.,

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Patent Owner.

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IPR2025-00015

10

U.S. Patent No. 10,036,012 B2

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DEPOSITION OF
ELI MEYER, PhD

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Goodwin Procter LLP
The New York Times Building
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New York, NY 10018

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10/10/2025
9:01 a.m. (EDT)

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REPORTED BY: MONIQUE CABRERA
JOB NO. 172167

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VIDEO-RECORDED DEPOSITION OF ELI MEYER, PhD,
held at Goodwin Procter LLP, The New York Times
Building, 620 Eighth Avenue, New York, NY, 10018,
before Monique Cabrera, Shorthand Reporter, and
Notary Public of the State of New York.

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1 I N D E X

2 WITNESS EXAMINATION BY PAGE

3 ELI MEYER, PhD MR. HOAGLAND-HANSON 5

4

5 E X H I B I T S

6 EXHIBIT DESCRIPTION PAGE

7 Petitioner's "Sequencing and de novo analysis of 9

8 Exhibit 1006 a coral larval transcriptome using

9 454 GSFlx".....

10 Petitioner's "An improved PCR method for walking 101

11 Exhibit 1007 in unclaimed genomic DNA".....

12 Petitioner's 5

13 Exhibit 1112 Eli Meyer Curriculum Vitae.....

14 Patent 56

15 Owner's

16 Exhibit 2080 Textbook.....

17 Patent 76

18 Owner's

19 Exhibit 2101 Redline of Eli Meyer declaration.....

20

21

22

1 ELI MEYER, PhD, called as a witness, having been
2 first duly sworn by a Notary Public of the State
3 of New York, was examined and testified as
4 follows:

5 THE WITNESS: I do.

6 COURT REPORTER: Can you state your
7 name for the record.

8 THE WITNESS: Eli Meyer.

9 MR. HOAGLAND-HANSON: Good morning,
10 Dr. Meyer.

11 THE WITNESS: Good morning.

12 MR. HOAGLAND-HANSON: And I don't
13 think we need appearances, so.

14 MS. CIPRIANO: No.

15 EXAMINATION

16 BY MR. HOAGLAND-HANSON:

17 Q. Okay. I am going to hand you what
18 I'm going to mark as Petitioner's Exhibit 1112.

19 (Whereupon, Petitioner's Exhibit
20 1112, Eli Meyer Curriculum Vitae, was marked
21 for identification.)

22 BY MR. HOAGLAND-HANSON:

1 Q. Just for the record, I think this is
2 now also going to be a patent owner's exhibit,
3 but this was the version I had on hand.

4 Dr. Meyer, this is a copy of your
5 curriculum vitae, correct?

6 A. That's right.

7 Q. And if you go to the last page, this
8 was last updated July 2025; is that right?

9 A. That seems correct.

10 Q. And did you prepare this CV?

11 A. I did.

12 Q. And was the CV prepared for the
13 purposes of this case?

14 A. No. This was a CV I used for job
15 applications.

16 Q. Okay. I want to start with your
17 professional profile section here on the first
18 page.

19 You are an accomplished marine
20 biologist; is that right?

21 A. That's right.

22 Q. That is your area of expertise,

1 right?

2 A. Yes.

3 Q. Okay. It says you are an expert in
4 coral biology, genomics, and environmental
5 physiology; is that right?

6 A. Yes, I think that's a fair
7 statement.

8 Q. Okay. And that's specific to your
9 work as a marine biologist, right?

10 A. Yes.

11 Q. Okay. You don't consider yourself
12 an expert in next-generation sequencing,
13 generally, do you?

14 A. I do, yes. I've used
15 next-generation sequencing throughout my entire
16 research career, starting from my first
17 publication.

18 Q. If you go to page 2, there is a
19 reference to your postdoctoral research work at
20 the University of Texas.

21 Do you see that?

22 A. I do.

1 Q. And your advisors for your
2 postdoctoral research were Professor Juenger and
3 Professor Matz; is that right?

4 A. That's right.

5 Q. And there are three bullets here.
6 The third bullet, you say you codeveloped a
7 2b-RAD genotyping method that was published in
8 "Nature Methods"; is that right?

9 A. That's right.

10 Q. Can you tell me about that method?

11 A. Sure. This is a method for genetic
12 analysis, looking at genetic variation between
13 organisms. It relies on next-generation
14 sequencing. And we developed both the laboratory
15 methods for preparing the sequencing libraries
16 and also, the analytical methods for analyzing
17 the data that comes out of that approach.

18 Q. How does the 2b-RAD method work?

19 A. It targets every site in the genomic
20 DNA that contains a specific restriction site. A
21 restriction site is a defined short DNA sequence
22 that's recognized by an enzyme called the

1 restriction enzyme.

2 And so this is a method of targeting
3 specific regions of the genome to evaluate
4 genetic variation at those regions.

5 So the -- it relies on
6 next-generation sequencing, but aside from that,
7 it's quite different from the approaches that
8 we're discussing here today.

9 Q. Why did you list this paper in
10 particular on your CV?

11 A. In a CV, there's often a motivation
12 to keep it short. I have about 42 publications,
13 and that takes up a lot of space and so this was
14 one of the highest impact. It was a paper
15 published in a high impact journal. And so that
16 was the motivation for highlighting it in the CV.

17 (Whereupon, Petitioner's Exhibit
18 1006, "Sequencing and de novo analysis of a
19 coral larval transcriptome using 454 GSFlx",
20 was identified.)

21 BY MR. HOAGLAND-HANSON:

22 Q. I am going to hand you a document

1 that was previously marked as Petitioner's
2 Exhibit 1006.

3 A. Okay.

4 Q. Do you recognize this document,
5 Dr. Meyer?

6 A. I do.

7 Q. This is a paper that you co-authored
8 in "BMC Genomics"?

9 A. That's right.

10 Q. You offer some opinions about this
11 paper in the declaration you submitted in this
12 case, right?

13 A. That's correct.

14 Q. You reviewed the paper carefully
15 when you prepared your declaration, right?

16 A. I did.

17 Q. Have you reviewed the paper again
18 this week?

19 A. Parts of the paper, yes.

20 Q. Is there anything in the paper that
21 you think is incorrect?

22 A. I don't recall anything that's

1 incorrect in the paper.

2 Q. Okay. Any statements in the paper
3 that you no longer agree with today?

4 A. No. I can't think of any.

5 Q. I want to ask you a couple of
6 background questions about the paper.

7 In the abstract, you say -- and I am
8 in the conclusion of the abstract.

9 Are you with me?

10 A. Yes.

11 Q. "The methods described here for deep
12 sequencing of the transcriptome should be widely
13 applicable."

14 Do you see that?

15 A. I do.

16 Q. And you agree with that?

17 A. So it's useful to read the whole
18 sentence. "Widely applicable to generate
19 catalogs of genes and genetic markers in emerging
20 model organisms."

21 Yes, so I still think that's the
22 entire sentence I would agree with.

1 Q. And these methods are not limited to
2 the particular coral that you sequenced in this
3 paper, right?

4 A. That's correct. They should be
5 generally applicable to any organism.

6 Q. This was a proof of concept study;
7 it's fair to say?

8 A. I would say there were two goals to
9 the paper. One is the method itself. And that,
10 you might categorize as a proof of concept paper.
11 But there was also the biological goal of the
12 study, which was to generate this resource for a
13 particular species that was widely studied in
14 coral biology. So I'd say both goals were
15 equally important to us.

16 Q. Okay. But the first goal was to be
17 a proof of concept for the particular library
18 preparation method that was disclosed, and that
19 goal was achieved, right?

20 A. Yes. It was to demonstrate how you
21 would produce these libraries and to evaluate how
22 well that method worked.

1 Q. And you're telling the scientific
2 community what happens when you use this
3 sequencing method, right?

4 MS. CIPRIANO: Objection. Form.

5 A. I guess I'm a little unclear. Could
6 you repeat the question?

7 BY MR. HOAGLAND-HANSON:

8 Q. What's the purpose of a scientific
9 publication?

10 A. To communicate the results of your
11 study.

12 Q. Okay. And here you're communicating
13 the results of this study to the scientific
14 community, right?

15 A. Yes, that's right.

16 Q. What's a transcriptome?

17 A. A transcriptome is a collection of
18 all of the expressed RNA sequences in an
19 organism.

20 Q. So it's less than all of the genetic
21 material in the organism, right?

22 A. That's right.

1 Q. It's not even all of the RNA in the
2 organism, right?

3 A. That's true.

4 Q. This is a method of selectively
5 sequencing just the transcriptome?

6 A. Yes.

7 Q. I want to go to page 2 of your
8 paper. This is where the "Results" section
9 starts.

10 Do you see that?

11 A. I do.

12 Q. And there's a subsection here titled
13 "454 sequencing, assembly, and sequence
14 analysis."

15 Do you see that?

16 A. I do.

17 Q. And "sequence analysis," that refers
18 to the bioinformatic scripts that are used to
19 evaluate the sequencing results; is that fair?

20 A. Yes. Generally the data that comes
21 out of a study like this, the data are in the
22 form of DNA sequences, which you can think of as

1 being like words.

2 They're series of base pairs or
3 letters. And so any analysis of those sequences
4 would follow under this heading of "sequence
5 analysis." That includes the bioinformatic
6 analysis using scripts.

7 Q. Okay. And you were primarily
8 responsible for the sequencing analysis in this
9 paper; is that right?

10 A. That's right.

11 Q. The first step that's described here
12 is to trim the sequence reads.

13 Do you see that?

14 MS. CIPRIANO: Objection to form.

15 A. We -- we do trim the sequencing
16 reads. I'm not seeing where it's the first step,
17 but perhaps that's not important. It is
18 certainly an early step.

19 Q. Okay. Well, let's go through it.
20 You say, "An overview of the sequencing assembly
21 is given in Table 1."

22 Do you see that?

1 A. I do.

2 Q. Okay. And then it says, "After
3 removal of adaptor sequences, 623,267 reads
4 remained."

5 A. Yes.

6 Q. Is removal of the adaptor sequences
7 trimming?

8 A. It is, yes.

9 Q. Was there a step prior to trimming
10 that you just didn't mention here?

11 A. I don't recall if quality control
12 happens before or after trimming. It's not very
13 important, the order of these operations. And I
14 am just not stating it because I don't recall
15 which step happened first.

16 Q. Okay. That's fine. You -- then you
17 say, "Size-Selection to remove outlier reads
18 (unusually long and unusually short) reduced this
19 to 134 Mb (599,248 reads..."

20 Do you see that?

21 A. I do.

22 Q. Okay. That's a typical step in this

1 kind of sequencing, right?

2 A. It is.

3 MS. CIPRIANO: Objection to form.

4 BY MR. HOAGLAND-HANSON:

5 Q. You would want to do that as part of
6 any sequencing method, it's fair?

7 A. I would say it depends on the
8 sequencing platform. Some sequencing platforms
9 produce a range of different read lengths. 454
10 is one of those platforms.

11 And so any time you're using 454
12 sequencing, it would be a typical step to do size
13 selection and remove reads with unusual lengths,
14 especially short reads.

15 Other sequencing platforms in
16 contrast produce identical read lengths for every
17 read, and so size selection would not be used in
18 those cases.

19 Q. What's an example of a sequencing
20 platform that produces identical read lengths for
21 every read?

22 A. Illumina or SOLiD, both produce

1 defined read lengths.

2 Q. What's of interest at the end of
3 this process is the -- is the trimmed and
4 cleaned-up data, not the raw sequencing file,
5 right?

6 MS. CIPRIANO: Objection to form.

7 A. I certainly agree that that -- the
8 -- the trimmed and cleaned-up data are what we
9 focused on, and that's what we draw our
10 biological conclusions from.

11 BY MR. HOAGLAND-HANSON:

12 Q. You say at the -- in the last
13 sentence of this paragraph, "The size
14 distribution for these trimmed, size-selected
15 reads is shown in Fig 2A, revealing that 92% of
16 trimmed reads fell between 100 and 300 bp in
17 length."

18 Do you see that?

19 A. I do.

20 Q. And the -- and figure 2A appears on
21 page 4?

22 A. Correct.

1 Q. Is there anything unusual about the
2 distribution of reads in figure 2A?

3 MS. CIPRIANO: Objection to form.

4 A. I guess defining it as unusual would
5 require that we compare it to something else. I
6 could discuss and describe this distribution, but
7 to evaluate if it's unusual, I'd have to ask what
8 we're comparing it to.

9 BY MR. HOAGLAND-HANSON:

10 Q. Why don't you discuss and describe
11 it.

12 A. Sure. So most of the reads, the
13 majority of this distribution, falls just under
14 300, a little under 270, but there is a -- a skew
15 to the left, to the lower read length. So it's
16 not a normal distribution. Rather, it's skewed.

17 Q. Do you discuss the skewed
18 distribution anywhere in your paper?

19 A. I don't recall any discussion of it.

20 Q. When was the first time that you
21 notice the skewed distribution?

22 A. Well, certainly very early in the

1 process, as soon as you look at the distribution
2 of read lengths.

3 Q. You didn't think it was relevant in
4 2009 when you wrote the paper?

5 A. And I still don't think it affected,
6 you know, the goals or conclusions of the paper.
7 I found this pretty typical for that kind of
8 data.

9 Q. You mentioned that the majority of
10 the distribution follows -- falls just under 300.
11 Why 300?

12 A. I'm curious what you mean by "why
13 300."

14 Q. Why did you use the number 300?

15 A. I'm looking at the graph and
16 approximating visually from the graph.

17 Q. What values are on the X axis in
18 your figure?

19 A. It says 70, and then it says 130.
20 That's followed by 200, 270, and 340.

21 Q. So not 300?

22 A. I'll note that 300 falls between 270

1 and 340.

2 Q. Yeah, I'm just wondering why you
3 picked 300 if it wasn't a value on the graph.

4 A. Commonly, when people discuss
5 numbers, they use round or whole numbers. It's
6 common strategy in discussing numbers.

7 Q. Is -- is 300 halfway between 270 and
8 340?

9 A. Would you like to do some math and
10 figure out? It's -- 300 is between 270 and 340.

11 Q. It -- it's fair to say here that the
12 -- almost all the reads are below 270, right?

13 A. Yeah. Would they also be below 300?

14 Q. You'd agree that they're below 270?

15 A. I do agree.

16 Q. Okay. What's the significance of
17 the skewed distribution here?

18 MS. CIPRIANO: Objection to form.

19 Scope.

20 A. It seems to me that -- that you are
21 drawing some significance from it that we have
22 not. I don't recall that we discussed any

1 significant conclusions from that distribution.

2 BY MR. HOAGLAND-HANSON:

3 Q. Well, I guess I'm -- I'm just trying
4 to figure out -- I -- I don't think I, in
5 fairness, introduced the concept of skewing here.
6 I think I asked you to discuss the data, and you
7 said it's not a normal distribution. It's
8 skewed.

9 A. Yeah, that's how I would describe
10 this distribution. If you weren't able to look
11 at the graph, if instead I was trying to convey
12 to you verbally, what does the graph look like, I
13 would have used the phrasing that I used in
14 discussing and describing it.

15 Q. Is there anything else that you need
16 to take into consideration when evaluating
17 figure 2A?

18 MS. CIPRIANO: Objection to form.

19 A. I'm not sure what you're getting at.

20 BY MR. HOAGLAND-HANSON:

21 Q. Was figure 2A generated from the
22 trimmed or untrimmed reads?

1 A. That is from the trimmed reads.

2 You'll notice the figure legend says it's after
3 removal of adaptor sequences and outliers.

4 Q. Do you know what the distribution
5 was prior to removal of adaptor sequences and
6 outliers?

7 A. I don't recall.

8 Q. Why didn't you provide that
9 distribution in your paper?

10 MS. CIPRIANO: Objection. Scope.

11 A. Generally when you are preparing a
12 scientific manuscript, there is an either an
13 applied or explicit length limit. You have a
14 certain amount of space, a certain number of
15 figures, and so you make priority decisions and
16 include the figures that you consider most
17 valuable.

18 We considered the trimmed and size
19 selected data to be more valuable than the
20 initial raw data, and so that's the one that we
21 showed.

22 BY MR. HOAGLAND-HANSON:

1 Q. I want to skip ahead a bit to pages

2 6 and 7. On page 6, there is a subheading

3 "Pathways and complexes."

4 Do you see that?

5 A. I see that.

6 Q. And in this section, you provide
7 some discussion of the coverage that you got in
8 your sequencing data for certain known genes. Is
9 that a fair summary?

10 A. I might not use the word "coverage."
11 I might use a term like "the presence of certain
12 genes in our dataset."

13 Q. And you go on to discuss in this
14 section that some genes weren't present; is that
15 fair?

16 A. Yes. There were some genes that we
17 looked for and did not find.

18 Q. One of which was activin-like
19 kinase?

20 A. Could you show me where you're
21 seeing that?

22 Q. Sure. I am in the paragraph -- the

1 partial paragraph on page 7, in the left-hand
2 column, "Activin-Like kinase was notably absent
3 from this list."

4 A. I see this.

5 Q. And just for the reporter's benefit,
6 activin is A-C-T-I-V-I-N.

7 Did I spell it correctly?

8 A. Correct.

9 Q. Okay. And so you didn't detect the
10 presence of the activin-like kinase gene, right?

11 A. Correct.

12 Q. And you provide some reasons why
13 that gene may not have been present.

14 Do you see that?

15 A. I do.

16 Q. And the two possible explanations,
17 one would be that the gene is not expressed,
18 right?

19 A. Correct.

20 Q. And another possible explanation is
21 the gene is expressed at a very low level, right?

22 A. Correct.

1 Q. And if the gene was expressed at a
2 very low level, there's the possibility that that
3 particular fragment doesn't get the right
4 adaptors ligated to it, and so it's not
5 amplified; is that right?

6 MS. CIPRIANO: Objection.
7 Incomplete hypothetical.

8 A. I will say without getting into the
9 specific steps at which the gene may fail to be
10 captured, I will agree with the statement that a
11 gene expressed at sufficiently low levels could
12 fail to make it through to the final data set.

13 BY MR. HOAGLAND-HANSON:

14 Q. If that particular gene does not get
15 the right adaptor sequences appended to it, it
16 won't amplified as part of your library
17 preparation, right?

18 MS. CIPRIANO: The same objection.

19 A. If the fragment of cDNA does not get
20 ligated to the right adaptors, it would not be
21 amplified or make it into our data.

22 BY MR. HOAGLAND-HANSON:

1 Q. And one of the reasons why it
2 doesn't make it into the data is the amplified
3 sequences will vastly outnumber that solitary
4 fragment, right?

5 MS. CIPRIANO: Objection to form.

6 A. If it's not ligated, it would not be
7 amplified at all. If the adaptors do not ligate
8 to the fragment, that fragment would not be
9 amplified at all. And it would not make it into
10 the final data.

11 BY MR. HOAGLAND-HANSON:

12 Q. Okay. In the next paragraph, you
13 also note, "A similar search was conducted for a
14 set of transcript" -- let me try that one more
15 time -- "transcription factors known to be
16 present in *N. vectensis*, based on conserved
17 domains characteristic of each transcription
18 factor family."

19 Do you see that?

20 A. I do.

21 Q. And you say, "Of the 20 families
22 investigated, these searches identify annotated

1 sequences corresponding to 18" of the 20
2 families, right?

3 A. Yes.

4 Q. And then again, at the -- at the
5 bottom of this column, you say, "The lack of
6 detection of these genes is not evidence that
7 they are absent in the coral larvae."

8 Do you see that?

9 A. I do.

10 Q. And then you say, "it might indicate
11 their low expression, incomplete sequencing
12 coverage, or inadequate annotation."

13 Is that right?

14 A. Yes.

15 Q. And if the cause was low expression,
16 then the same phenomenon that we just talked
17 about with respect to the activin-like kinase
18 gene could occur, right?

19 A. Yes. Regardless of the type of gene
20 we are discussing, any gene that's present at a
21 sufficiently low level could fail to be captured
22 in the final data.

1 Q. I want to skip ahead to page 9 now.

2 There is a section in the left-hand
3 column called "SNP detection and validation."

4 A. Yes.

5 Q. And it says "SNP," but they usually
6 say "snip," right?

7 A. That's right.

8 Q. And that's a single nucleotide
9 polymorphism?

10 A. That's right.

11 Q. What was the purpose of the
12 experiment that you are describing in this
13 section?

14 A. When you sequence DNA that comes
15 from a pool of multiple individuals, as we did in
16 this study, the sequence data can contain genetic
17 polymorphisms. These are regions of a genome
18 that differ among those individuals in the pool.

19 Researchers may be interested to
20 look at those polymorphisms in a sequence dataset
21 and ask the question: Are they biologically
22 real, or are they some kind of artifact or error

1 of the sequencing process? And so our goal
2 evaluating these SNPs was to ask the question:
3 When you observe SNPs in a 454 sequenced dataset,
4 are they biologically real, and therefore, useful
5 for follow-up studies of genetic variation?

6 Q. Did this experiment involve
7 enriching for any particular sequences?

8 MS. CIPRIANO: Objection to form.

9 A. We were not enriching for any
10 particular sequence in terms of particular genes
11 or families of genes. We were enriching for
12 expressed genes; that is, mRNA as compared to any
13 of the other nucleic acids in an organism.

14 BY MR. HOAGLAND-HANSON:

15 Q. Okay. In the right-hand column,
16 there's the start of the "Discussion" section of
17 your paper.

18 A. Yes.

19 Q. And there is a section with the
20 subtitle "Methodological advances for 455
21 sequencing of transcriptomes."

22 Do you see that?

1 A. Yes.

2 Q. And you say, "The methods described
3 here resolve several challenges associated with
4 454 sequencing of transcriptomes."

5 A. Correct.

6 Q. And you go on to describe what those
7 challenges were in this second paragraph [sic];
8 is that fair?

9 A. That's right.

10 Q. And the first challenge was that
11 "454 sequencing does not efficiently process
12 homopolymer regions greater than 8 bp in length."

13 A. Correct.

14 Q. And the result of that is "the
15 poly-A tails of the 3' ends of intact transcripts
16 present a problem, and would be expected to
17 result in under-representation of the 3' ends of
18 transcripts."

19 Is that right?

20 A. Correct.

21 Q. And you don't want
22 underrepresentation of the 3' ends; is that fair?

1 MS. CIPRIANO: Objection. Form.

2 A. The goal of our sequencing was to
3 sequence the entire length of each transcript,
4 from the 5' end to the 3' end, and so any part of
5 the transcript was equally valuable to us,
6 including the 3' end. We did not want to miss
7 those data.

8 BY MR. HOAGLAND-HANSON:

9 Q. The 3' end of complete mRNA
10 transcripts have the poly-A tail, right?

11 A. Correct.

12 Q. And the sequence that's adjacent to
13 the poly-A tail is biologically relevant, right?

14 A. Yes.

15 Q. And when you are sequencing a
16 transcriptome, you are interested in the sequence
17 that's adjacent to the poly-A tail, right?

18 A. That's correct. The sequence of the
19 poly-A tail itself is not interesting.

20 Q. Right. But sequence that is right
21 next to the poly-A tail is interesting?

22 A. Correct.

1 Q. And the position of the poly-A tail
2 tells you where the transcript starts or ends
3 depending on which way you're thinking about it?

4 A. Yes. I guess I would phrase it as
5 "end" but, yes.

6 Q. Okay. It's interesting to know
7 where the transcript ends, right?

8 A. Correct.

9 Q. You say here that you solved this
10 underrepresentation problem by -- well, let me
11 ask a complete and better question.

12 With respect to the
13 underrepresentation problem, you say, "In our
14 method, this problem is resolved by simply
15 interrupting the poly-T region with a single C."

16 Is that right?

17 A. Correct.

18 Q. Okay. So your library preparation
19 method solved the underrepresentation problem at
20 the 3' end?

21 MS. CIPRIANO: Objection to form.

22 A. Solved the underrepresentation

1 problem at the 3' end?

2 I do that's -- I do think that's
3 fair, yes.

4 BY MR. HOAGLAND-HANSON:

5 Q. And then you describe the -- a
6 second challenge associated with 454 sequencing
7 of transcriptomes. You say, "Another difficulty
8 in 454 transcriptome sequencing is concatenation
9 of adaptors during cDNA preparation."

10 A. That's correct.

11 Q. And your library preparation method
12 solved that problem, too?

13 A. Correct.

14 Q. These two problems that you describe
15 here, they're not entirely unique to
16 454 sequencing, right?

17 MS. CIPRIANO: Objection. Form.

18 A. These two problems, following the
19 phrase "another difficulty," is that the two
20 problems?

21 BY MR. HOAGLAND-HANSON:

22 Q. So, sorry. We talked about the

1 first problem is underrepresentation of the 3'
2 ends.

3 A. Okay.

4 Q. And then the second problem is
5 adopter concatenation, right?

6 A. I see.

7 So the first problem, the
8 homopolymer problem, differs among sequencing
9 platforms in terms of how much of a problem it
10 is. It was a well-described problem for 454. It
11 is not a problem for many other next-gen
12 sequencing methods that have followed.

13 I believe there is another platform
14 that it is a problem for, but I haven't used it
15 myself. So I can't speak with any certainty
16 about that.

17 The second problem that we're
18 discussing here, the concatenation, that would be
19 a problem across sequencing platforms.

20 Q. You don't mention any other
21 challenges that your method was designed to
22 resolve, do you?

1 A. Perhaps not in this paragraph, but
2 there are other steps we took to resolve
3 challenges with transcriptome sequencing.

4 Q. You didn't talk about any of them in
5 your paper in 2009?

6 MS. CIPRIANO: Objection to form.

7 A. I would be happy to look through the
8 paper and point you to them, but I believe we do
9 discuss them. Perhaps it would only be in the
10 methods section, or I could discuss them here
11 verbally.

12 BY MR. HOAGLAND-HANSON:

13 Q. No, take your time. I would like
14 you to point me to where in your paper you talk
15 about them.

16 A. Sure. So I'll point you to one
17 example on page 13. On the left-hand column, the
18 third paragraph down, you will see that this
19 paragraph begins with, "To minimize differences
20 among the abundance of different transcripts
21 (i.e., genes expressed at different levels)," we
22 use the following kit, paraphrasing.

1 So the -- the beginning of this
2 sentence illustrates one of these other
3 challenges that we addressed in our study, which
4 is, some genes are present at a high copy number
5 in the pool of RNA. They're highly expressed.
6 Other genes are expressed at a low level. And
7 that variation in expression level is a challenge
8 for producing a comprehensive sequence database.

9 In this case, we used a commercially
10 available kit. It was not an innovation of our
11 own, but nevertheless, it was a step we took to
12 address a challenge in transcriptome sequencing.

13 Q. Are there any other challenges that
14 you talk about in your paper?

15 A. There are, and I can search to find
16 the reference for them or do it verbally. Would
17 you prefer?

18 Q. No, I would like to see where they
19 are in the paper, please.

20 A. Sure. Sure.

21 Well, for completeness, let's
22 include this one. So we'll start on page 12.

1 And I'm sorry, it's only one word on page 12, the
2 last word "RNA." And then that sentence
3 continues on to page 13, "RNA preparations were
4 purified by precipitation with lithium chloride
5 prior to cDNA synthesis."

6 The reason I'm highlighting this
7 sentence is it illustrates how we solved another
8 challenge for transcriptome sequencing, which is
9 the necessity of removing DNA from the -- from
10 the biological material to purify only the RNA.

11 Now, that isn't spelled out in
12 detail in the paper because it's a very standard
13 method in molecular biology and the reader would
14 have understood that this was the purpose for
15 that study.

16 Q. It's not a challenge that you
17 identified, though, at the time of the paper,
18 right?

19 MS. CIPRIANO: Objection. Form.

20 A. It's not a challenge that emerged
21 from our data. It's a challenge that we knew
22 existed for any transcriptome sequencing, and so

1 we took this commonly used step to address that,
2 that well-known challenge.

3 BY MR. HOAGLAND-HANSON:

4 Q. Are there any other challenges that
5 you discuss in your paper?

6 A. Yes, and I'm looking for a good --
7 good reference for that.

8 I think the third challenge -- for
9 this -- whatever the number is that we're on. I
10 think the other challenge that I wanted to
11 discuss is probably best illustrated in a -- the
12 diagram shown in figure 1. So that is on page 3
13 of the manuscript.

14 And this -- this figure includes a
15 lot of data that I'm not calling your attention
16 to at the moment, although I'd be happy to answer
17 questions.

18 My purpose for calling your
19 attention to this figure is that this figure
20 illustrates the concept of PCR suppression, which
21 is a phenomenon that we take advantage of at
22 several places in this protocol.

1 And generally, PCR suppression
2 inhibits the amplification of any short sequences
3 that contained complementary sequences on their
4 ends, the 5' and 3' ends.

5 Those complementary sequences can
6 hybridize together, as shown in the bottom
7 right-hand corner of this figure, where you see
8 structures that we term "hairpin structures."
9 The two complementary regions are hybridized like
10 this, and the intermediate sequence is a loop
11 between them.

12 The formation of that structure
13 inhibits amplification of that molecule, and so
14 it doesn't show up in the final sequence pool.
15 The reason I'm calling your attention to this is
16 it's a phenomenon we took a -- we took advantage
17 of at several stages in our protocol.

18 And the challenge that I'm
19 highlighting here is the challenge that short
20 fragments, inherently, have a tendency to amplify
21 very strongly in PCR. They produce a lot of
22 product in PCR. They amplify well. Long

1 fragments have a tendency to not amplify well.

2 And so the challenge is a bias
3 towards short fragments. And so we use PCR
4 suppression as a mechanism to counter that
5 challenge, that tendency to overamplify short
6 fragments.

7 Q. Any other challenges that you talk
8 about in your paper?

9 A. I don't recall another one off the
10 top of my head. But if you have another one in
11 mind, I'd be happy to talk about it.

12 Q. You have reviewed your paper
13 carefully and recently. Is that fair to say?

14 A. That's fair to say.

15 Q. And you do not recall any other
16 challenges that you discuss in the paper; is that
17 fair?

18 MS. CIPRIANO: Objection to form.

19 A. It sounds as if you may be recalling
20 one that's not coming to mind for me at the
21 moment. If you'd like to remind me of it, I'd be
22 happy to discuss it.

1 BY MR. HOAGLAND-HANSON:

2 Q. You don't recall any others?

3 MS. CIPRIANO: Objection. Form.

4 A. At the moment, no other challenges
5 are coming to mind.

6 BY MR. HOAGLAND-HANSON:

7 Q. I want to go back to page 9, the
8 paragraph of the discussion section, talking
9 about the challenges that we were looking at a
10 moment ago.

11 In your discussion of the
12 underrepresentation issue with the 3' ends, you
13 provide some discussion of how you confirmed that
14 that problem was resolved, right?

15 A. Yes.

16 Q. And you provide some data to support
17 your conclusion that you resolved the 3'
18 sequencing problem, right?

19 A. Yes.

20 Q. And in the middle of the paragraph
21 you say, "A single copy of this 'broken-T'
22 adaptor was found in 98,276 of the raw reads

1 (16% of the total), slightly more than the
2 expectation approximately (~10%) based on average
3 read length (232 bp) and assuming an average
4 transcript size of 2,200 bp."

5 A. Correct.

6 Q. That calculation was designed to
7 demonstrate that you had resolved the
8 underrepresentation of the 3' ends, right?

9 A. That's correct.

10 Q. Were you responsible for this
11 calculation?

12 A. It's a very simple calculation,
13 simply division of one number by another. I
14 don't recall if Dr. Matz or I was the first to do
15 that simple calculation. I wrote the first draft
16 of the manuscript, and I believe this was in that
17 first draft, but I can't recall 16 years ago
18 which version of the manuscript that entered in.

19 Q. Sitting here today, your
20 recollection is these are your words?

21 A. They're certainly my words.

22 Q. This calculation's reasonable,

1 right?

2 MS. CIPRIANO: Objection to form.

3 A. I obviously thought it was
4 reasonable, and my co-authors agreed because we
5 included it. There are nuances worth discussing
6 about the statement, but I stand by the statement
7 as written.

8 BY MR. HOAGLAND-HANSON:

9 Q. It's based on reliable assumptions?

10 MS. CIPRIANO: Objection to form.

11 A. What assumptions are you referring
12 to?

13 BY MR. HOAGLAND-HANSON:

14 Q. What's the calculation based on?

15 A. Sure. Let's walk through it. So we
16 say a single copy of this adaptor was found in a
17 little over 98,000 of the raw reads. In
18 parentheses, we say this is 16 percent of the
19 total. The way that number was determined is
20 simply dividing a little over 98,000 by the total
21 number of reads. So that's a very
22 straightforward calculation with no assumptions

1 revolved -- involved. It's simply arithmetic.

2 The second part of the sentence says
3 this is slightly more than the expectation,
4 approximately 10 percent, based on two numbers,
5 an average read length, and those are data from
6 our study shown in a previous table. The average
7 read length in our study was 232.

8 To arrive at 10 percent, you divide
9 232 by this average transcript size of 2200 base
10 pairs. And it's that final number, the 2200 base
11 pairs, that's based on assumptions.

12 At the time of writing this study,
13 it was unknown what is the true transcript length
14 for this coral species. And so we had to pick a
15 reasonable transcript -- transcript length found
16 in other animals. This was a part of general
17 knowledge among biologists at the time. And so
18 we simply plugged in this number, this assumption
19 of 2200 base pairs.

20 So in talking through that sentence,
21 what I'm trying to illustrate is the difference
22 between some numbers, which are based on our data

1 and measurements and this final number, which is
2 almost pulled out of the air from general
3 knowledge. We -- we considered it a -- a
4 reasonable assumption for what a transcript
5 length might be.

6 Q. Before we talk about the
7 denominator, I want to talk about the numerator,
8 the 232.

9 A. Sure.

10 Q. That number is based on the data
11 that you generated, right?

12 A. That's correct.

13 Q. And so that number is not an
14 assumption, right?

15 A. Correct.

16 Q. You don't have any reason sitting
17 here today to think that you should have used a
18 different number for the numerator, right?

19 A. Correct.

20 Q. So I want to talk about the
21 assumption of the average transcript size now,
22 the 2200 base pairs.

1 A. Yes.

2 Q. That was a reasonable assumption at
3 the time. Right?

4 A. I certainly think so.

5 Q. If you were writing this paragraph
6 today, would you use a different number?

7 MS. CIPRIANO: Objection. Scope.

8 A. If I were writing this paragraph
9 today, my approach would be to review the current
10 literature and evaluate what is the best
11 assumption we could make.

12 I wouldn't rely on pulling it from
13 memory, and that's why I'm hesitant to say if I
14 would use a different number or not. I would --
15 I would look at the existing literature in 2025
16 and determine what's the best assumption I could
17 make.

18 BY MR. HOAGLAND-HANSON:

19 Q. Okay. You haven't done that
20 analysis?

21 A. No, I haven't.

22 Q. Why not?

1 MS. CIPRIANO: Objection to form.

2 Scope.

3 A. 16-year-old paper, there's no --
4 there's no -- there's no cause for it. I have
5 not been asked to do that.

6 BY MR. HOAGLAND-HANSON:

7 Q. Is that a difficult analysis?

8 MS. CIPRIANO: Objection to form.

9 A. Is it a difficult analysis? I would
10 say it would take some time, and all of our time
11 is limited, and we have to prioritize giving our
12 time to projects that have a benefit or
13 motivation.

14 There may be some curiosity driving
15 a person to do that analysis, but I haven't had
16 the free time to do things like that just out of
17 curiosity. So lacking any professional
18 motivation for it, I haven't revisited that
19 question.

20 BY MR. HOAGLAND-HANSON:

21 Q. You don't have any reason sitting
22 here today to use any other number; that's fair?

1 MS. CIPRIANO: Objection to form.

2 A. I'll -- I'll just restate that if I
3 were to use a different number, it would have to
4 be based on a search of the current scientific
5 literature, and I don't know what that number
6 would be. So I don't know if it would be different
7 or the same.

8 BY MR. HOAGLAND-HANSON:

9 Q. Sitting here today, 2200 is as
10 accurate a number as any other number, right?

11 MS. CIPRIANO: Objection. Form.

12 Asked and answered.

13 A. I think it was a reasonable number
14 for us to choose in 2009 when we wrote the paper,
15 and that's really the only bar that one has to
16 meet in writing a scientific paper.

17 BY MR. HOAGLAND-HANSON:

18 Q. I think you were briefly looking up
19 some parts of the "Method" section a minute ago,
20 but I just want to take a look at that. That
21 starts at page 12.

22 A. Okay.

1 Q. And I want to skip ahead a bit --
2 well, at the -- at the bottom of page 12, in the
3 right-hand column, there's a subsection that
4 starts "Preparation of cDNA samples."

5 Do you see that?

6 A. I see that.

7 Q. And it -- and it goes on for a ways
8 until the end of that section at the top of 14.

9 A. I see that.

10 Q. It says, "A step-by-step protocol
11 for the library preparation method outlined above
12 is provided in the additional files accompanying
13 this article (additional file 4)."

14 Do you see that?

15 A. I see that.

16 Q. And if you look at the -- the
17 document that you're holding that's been
18 previously marked as Petitioner's Exhibit 1006,
19 and you go to the end of your -- your paper, and
20 it's marked -- this wasn't paginated originally,
21 but there's a page number at the bottom, page 19.

22 Do you see that?

1 A. I see that.

2 Q. This is the protocol additional file
3 4, right?

4 A. That's correct.

5 Q. Were you also responsible for
6 writing additional file 4?

7 A. I believe the first draft of this
8 additional file was prepared by co-authors, but I
9 reviewed and edited, if necessary.

10 Q. Okay. I want to go back to -- to
11 page 14. You say, "That protocol" -- meaning the
12 additional file 4 protocol -- "includes minor
13 modifications that we have recently developed to
14 reduce the number of manipulations required,
15 improve reproducibility, and to further reduce
16 adaptor concatenation."

17 Do you see that?

18 A. I see that.

19 Q. And then you recommended that
20 protocol to the researchers, right?

21 A. Correct.

22 Q. So you'd expect someone reading your

1 manuscript to follow the protocol in additional
2 file 4, right?

3 A. This -- this was our recommendation.

4 Q. You would expect to get comparable
5 sequencing results regardless of whether the
6 additional minor modifications were used, right?

7 MS. CIPRIANO: Objection to form.

8 A. I would say the -- the results
9 should be overall very similar, but we do
10 highlight some improvements in that modified
11 protocol that would be detectable in the data,
12 primarily in the raw data, rather than the final
13 assembly dataset.

14 BY MR. HOAGLAND-HANSON:

15 Q. It's fair to say that the results
16 that you disclose in your paper are
17 representative of the method with or without the
18 modifications, right?

19 MS. CIPRIANO: Objection to form.

20 A. I think that -- I think that's a bit
21 of an assumption. The data presented in the
22 paper were generated using the method that is

1 outlined in the main body of the text.

2 I think it's reasonable to believe
3 that if you repeated it exactly with the modified
4 protocol, you would get very similar and
5 comparable results. However, I have not done
6 that, and so I can't say that with any certainty.

7 BY MR. HOAGLAND-HANSON:

8 Q. Did you ever prepare a library for
9 sequencing using the additional file 4 protocol?

10 A. Personally, I have not. My
11 co-authors on the manuscript used those
12 modifications. Basically, while I was preparing
13 this manuscript, they were making minor
14 modifications to the protocol.

15 Q. Okay. And which co-authors are you
16 referring to?

17 A. That would be Dr. Matz and
18 Dr. Aglyamova. She is the second author on the
19 paper.

20 Q. And that's A-G-L-Y-A-M-O-V-A,
21 correct?

22 A. Correct.

1 Q. Why did you add additional file 4 to
2 your manuscript?

3 MS. CIPRIANO: Objection to form.
4 Scope.

5 A. This was our recommendation to
6 researchers who would use our protocol.

7 Why did we add it? This was a
8 matter of some discussion. Should we add the new
9 modified protocol or only include the original
10 protocol?

11 The argument that ultimately was
12 compelling was that if we were to reproduce this
13 study ourselves, if we were to be motivated to
14 conduct exactly this study a second time, we were
15 convinced that the modified protocol would
16 produce better results.

17 And so our feeling was if that's the
18 advice we would take ourselves, then we should
19 also give that advice to the rest of the
20 scientific community.

21 BY MR. HOAGLAND-HANSON:

22 Q. Are you aware of any publications

1 that provide results using the additional file 4
2 method?

3 A. I am not certain. I couldn't
4 provide you with a comprehensive list of the
5 publications that have used that.

6 These sequencing technologies evolve
7 fairly rapidly, and so my own use of 454 did not
8 last much longer beyond this paper.

9 Q. You are not a big fan of big bags of
10 oil?

11 MS. CIPRIANO: Objection to form.

12 A. I'm afraid I am not sure where the
13 question is going.

14 MS. CIPRIANO: We have been going
15 for about an hour. Is this good time for a
16 break?

17 BY MR. HOAGLAND-HANSON:

18 Q. Dr. Meyer?

19 A. I would take a quick break to grab a
20 cup of coffee. Maybe five minutes?

21 (Whereupon, a brief recess was
22 taken.)

1 BY MR. HOAGLAND-HANSON:

2 Q. Dr. Meyer, I am going to hand you
3 what has been previously marked as Patent Owner's
4 Exhibit 2080.

5 (Whereupon, Patent Owner's Exhibit
6 2080, Textbook, was identified.)

7 BY MR. HOAGLAND-HANSON:

8 Q. Do you recognize this document,
9 Dr. Meyer?

10 A. I do.

11 Q. What is it?

12 A. This was the source that we believe
13 the value of 2200 was derived from. So that
14 really was the primary reason for including this.
15 When I say, "2200," I mean the average transcript
16 length from our previous discussion.

17 Q. You said "we believe."
18 Who do you mean by "we"?

19 A. I'm sure you're familiar with the
20 history of the declaration, but I'll state for
21 the record that the first version of the
22 declaration was prepared by Dr. Matz, and he was

1 the one that actually identified this reference
2 for that version of the declaration. I reviewed
3 the declaration, including the statement, and
4 this references as the appropriate reference and
5 agreed with -- agreed with its conclusion.

6 Q. So I just want make sure that I
7 understand.

8 Do you have an independent
9 recollection of referring to this textbook?

10 A. I believe I said before, but if not,
11 I'll say clearly that the reason for choosing
12 that value of 2200 was based on verbal
13 conversations between Dr. Matz and I, 16 years
14 ago.

15 You'll notice that in the paper, we
16 do not provide a reference for the 2200 number,
17 and that's because we were drawing it from
18 general knowledge at the time.

19 Q. It's your testimony that the 2200
20 number came from general knowledge at time; is
21 that right?

22 A. Correct. And we believe that

1 this -- this references an appropriate resource
2 to demonstrate that it was part of the general
3 knowledge at the time.

4 Q. And you said "we" again. I just
5 want to -- I just want to make sure that I
6 understand.

7 Do you have any independent
8 recollection of referring to this textbook?

9 MS. CIPRIANO: Objection to form.

10 A. As -- as I said, I believe that the
11 reason I included 2200 in the manuscript was
12 because Dr. Matz and I had had verbal
13 conversations at the time based on our general
14 knowledge of biology.

15 BY MR. HOAGLAND-HANSON:

16 Q. Okay. I want to just make sure that
17 the record is clear.

18 You don't remember referring to this
19 textbook, right?

20 MS. CIPRIANO: Objection. Form.

21 A. The decision to include 2200 was
22 based on a verbal conversation, not sitting down

1 with textbooks and identifying references.

2 BY MR. HOAGLAND-HANSON:

3 Q. If you go to the second page of this
4 exhibit, there is a copyright date.

5 Do you see that?

6 A. I do.

7 Are we looking at 1994?

8 Q. Yeah. Where were you in 1994?

9 A. Where was I in 1994?

10 MS. CIPRIANO: Objection to form.

11 A. I would have been just beginning in
12 my undergraduate.

13 BY MR. HOAGLAND-HANSON:

14 Q. Do you recall ever referring to this
15 textbook before this case?

16 A. This is a widely used -- this is a
17 widely used textbook in molecular biology. I --
18 I can't point to you a specific time that I have
19 referred to this textbook, but it certainly was a
20 textbook that we were all familiar with at the
21 time that we worked on this study.

22 Q. The textbook was 15 years old at the

1 time that you did the study, right?

2 A. That sounds about right.

3 Q. Were there are more up-to-date
4 sources you could have referred to in 2009 than a
5 15-year old undergraduate textbook?

6 MS. CIPRIANO: Objection to form.

7 A. General knowledge is often informed
8 by older literature, not just the latest
9 literature. Much of scientific data is entered
10 into the general knowledge and remains there.

11 I don't see any problem with
12 referring to an older textbook for a statement of
13 general knowledge, but if you had been a reviewer
14 on our paper, you certainly would have been
15 within your rights to comment on references that
16 we included or did not include.

17 BY MR. HOAGLAND-HANSON:

18 Q. Is it fair to say that the reliance
19 on this textbook -- well, let me try that again.

20 Can you point me to where in this
21 Exhibit 2200 is mentioned?

22 A. Sure. So the page numbers for the

1 exhibit described this at page 13 of 28, and if
2 you go to the bottom of table 23.1, you will see
3 that the average mRNA length for mammals is
4 recorded at 2.2 kb, which is would be 2200 base
5 pairs.

6 Q. You don't have any independent
7 recollection of referring to this table when you
8 were drafting your paper, right?

9 A. As I've said, our process with
10 drafting the paper was based on general
11 knowledge, not any specific references.

12 Q. So if you had not received
13 Dr. Matz's declaration that said it came from
14 this textbook, you never would have gotten to
15 this textbook, right?

16 MS. CIPRIANO: Objection. Form.

17 A. I could only speculate about
18 something like that. If I had not received it
19 but had been requested to find a reference
20 myself, I may or may not have identified the same
21 reference. It was a part of general knowledge,
22 and so that number likely appears in many

1 different resources.

2 BY MR. HOAGLAND-HANSON:

3 Q. You mentioned that you don't cite
4 this textbook in your paper, right?

5 A. Correct.

6 Q. Do you think it would have struck
7 the editors of "BMC Genomics" as odd that, in
8 your paper on marine biology, you've got the
9 average transcript size from a 15-year-old
10 textbook table about the average transcript
11 length in mammals?

12 MS. CIPRIANO: Objection to form.

13 A. Well, I will note, we included
14 56 references in this manuscript. When you're
15 preparing a scientific manuscript, there is often
16 an implied or explicit length limit, and so
17 authors make priority decision about which
18 statements to provide references for and which
19 statements you can rely on general knowledge.

20 We made the judgement call at the
21 time that this was an appropriate statement to
22 base on general knowledge. Our reviewers, three

1 independent reviewers, none of them raised any
2 objections to leaving it uncited and the editor
3 did not, so I'll stand by their judgment.

4 BY MR. HOAGLAND-HANSON:

5 Q. Right. They said 2200 was
6 reasonable transcript length for coral, right?

7 MS. CIPRIANO: Objection.

8 Speculation.

9 A. They -- I -- I can say they -- no
10 one raised the objection that we needed a
11 citation for that number. Whatever motivation
12 they had for not objecting to it, no one raised
13 an objection to leaving the statement without a
14 citation.

15 BY MR. HOAGLAND-HANSON:

16 Q. You didn't say in your paper, the
17 transcript length of 2200 based on the general
18 knowledge and understanding of the average
19 transcript length in mammals, right?

20 MS. CIPRIANO: Objection to form.

21 A. That's right. Again, I'll refer to
22 the decisions authors have to make about the

1 length of a manuscript. We often prioritize
2 being concise. And so sometimes it's possible to
3 say it in a fuller and more detailed way and the
4 authors choose to say it in a concise way. That
5 was our choice here.

6 BY MR. HOAGLAND-HANSON:

7 Q. I just want to make sure I
8 understand your testimony today, Dr. Meyer.

9 It's your testimony that a person
10 reading the sentence that we were talking about
11 earlier on page 9 of your paper would understand
12 it to conclude with, assuming an average
13 transcript size of 2200 base pairs, parentheses,
14 based on the average length of the mammalian mRNA
15 transcript?

16 A. I'm sorry, could you clarify? What
17 is the question in that?

18 Q. I think you said that -- your
19 testimony was, you, the author, chose to say this
20 in a concise size way; is that fair?

21 A. That's fair.

22 Q. Okay. And the longer version that

1 you are saying a reader would understand from
2 this is that they would read this as assuming an
3 average transcript size of 2200 base pairs,
4 parentheses, based on the general knowledge that
5 an average transcript size of 2200 base pairs is
6 based on the average length of a mammalian
7 transcript?

8 MS. CIPRIANO: Objection to form.

9 A. I think your introduction of the
10 term "mammalian transcript" into that sentence is
11 not necessarily something that we were relying on
12 or that the reader would assume.

13 The statement, as written, assuming
14 an average transcript size of 2200 base pairs,
15 without any qualifiers, I think the reasonable
16 assumption -- the reasonable interpretation,
17 rather, of that sentence is that this is a
18 general average overall transcript length.

19 We didn't mention anything about
20 mammals in that sentence.

21 BY MR. HOAGLAND-HANSON:

22 Q. Dr. Meyer, when did you first learn

1 about this case?

2 A. I can't recall the specific date,
3 but I would say it was a couple months ago.

4 Q. Who first contacted you?

5 A. Dr. Matz contacted me with a very
6 brief e-mail, asking if I would be willing to
7 assist with this. When I replied with a "yes,"
8 he put me in contact with counsel.

9 Q. Before that e-mail you got from
10 Dr. Matz, when was the last time you had spoken
11 to him?

12 A. It had been quite some time. I had
13 to review my records in preparation to answer
14 that question. I now see it was late 2024, an
15 e-mail about an unrelated research matter was
16 our -- our most recent contact before this
17 e-mail.

18 Q. Did you have a -- have you spoken
19 with Dr. Matz on the telephone?

20 A. No contact at all with him other
21 than that e-mail chain.

22 Q. About this or anything else?

1 A. Not this or anything else.

2 Q. Have you subsequently talked to
3 Dr. Matz on the telephone?

4 A. I haven't had any contact with him
5 since he put me in contact with counsel.

6 Q. Are you being paid for your time
7 working on this matter?

8 A. Sure, I'm being compensated.

9 Q. How much?

10 A. I believe 250 an hour.

11 Q. Have you invoiced your lawyers for
12 your work on this case?

13 A. I have not yet.

14 Q. Do you expect to?

15 A. I do expect to. This is my first
16 time serving in a deposition, so many of the
17 logistical details are unclear to me, including
18 the details of invoicing.

19 Q. So you have not invoiced them yet
20 for the time you spent working on your
21 declaration either?

22 A. That's correct.

1 Q. Do you expect to be paid for your
2 meetings with your lawyers?

3 A. It's my understanding that all my
4 time is compensated at that rate.

5 Q. And you expect to be paid for your
6 time sitting for deposition today, right?

7 A. That's my understanding. But as I
8 said, I'm inexperienced with the process. If my
9 understanding is incorrect, that wouldn't be
10 surprising.

11 Q. You're going to submit a single
12 invoice, basically, for this project?

13 A. That -- that's how I imagined it
14 would work. To be honest, I have not asked the
15 question about how the invoicing works. So
16 perhaps we'll have that discussion after today.

17 Q. Approximately how much do you expect
18 that invoice to be?

19 A. I haven't done the math yet, so I'm
20 not sure.

21 Q. Have you worked on this case for
22 more than ten hours?

1 A. I think that's fair.

2 Q. More than 20 hours?

3 A. So if we're counting all the
4 interactions with counsel, I believe we've had
5 about four meetings over Zoom, perhaps an hour
6 each. We had a prep session in person yesterday,
7 and we have today. And it's unknown how long
8 today goes.

9 It seems to me that number comes
10 somewhere in the ten to 20 hours range, but I'd
11 have to sit down with a pencil and paper and
12 really look at my records to get a precise
13 estimate.

14 Q. What about your time spent preparing
15 the declaration?

16 A. Yeah, I believe that's also
17 invoice-able. But, again, that's a question I --
18 you know, would ask counsel about the logistics.

19 Q. About how much time did you spend on
20 that?

21 A. There were about three hours of
22 preparation overall during the -- the Zoom

1 meetings and those prep sessions, and another two
2 hours of prep -- in preparation for these --
3 these in-person meetings.

4 Q. So, call it, 20 hours total is about
5 five grand?

6 A. This seems like a reasonable
7 approximation.

8 Q. Do you do work as an independent
9 consultant outside of this case?

10 A. I haven't. You -- you see my CV.
11 That -- that describes my professional
12 experience. I -- I have no consulting
13 experience.

14 Q. You own a business, right?

15 A. I do.

16 Q. Do you take a salary?

17 MS. CIPRIANO: Objection to form.

18 A. Because it is a single member LLC --
19 I apologize, I'm forgetting the correct business
20 term here. But no, I don't draw it formally as a
21 salary. It's simply gross revenue minus all the
22 expenses, and I get what's left.

1 BY MR. HOAGLAND-HANSON:

2 Q. About how much was that last year?

3 MS. CIPRIANO: Objection. Scope.

4 A. I would have to consult my tax
5 returns to be sure. It was an embarrassingly low
6 number. It's a small company.

7 BY MR. HOAGLAND-HANSON:

8 Q. Less than 50 grand?

9 A. It was.

10 Q. And you said you've never been an
11 expert witness before; is that right?

12 A. That's correct.

13 Q. Why did you agree to work on this
14 case?

15 MS. CIPRIANO: Objection to form.
16 Relevance.

17 A. This is a question I asked myself
18 during the long travel out here. The fact is, I
19 was asked by an old friend and colleague if I
20 could help out with this matter. It seemed like
21 an easy enough thing, so I agreed.

22 As the process has gone on, I

1 haven't encountered any obstacles that made me
2 say, no, I can't help out with it anymore. So
3 that's -- that's the -- the the main motivation
4 is simply that I was asked.

5 Now, if I want to be introspective
6 about it, every -- every scientist loves to get
7 some attention to their research and discuss
8 their research, even if it has no actual benefit
9 for themselves. So I'm generally available to
10 address questions about my research.

11 BY MR. HOAGLAND-HANSON:

12 Q. When you started your consulting
13 work on this case, was the first thing that you
14 were provided by your lawyers Dr. Matz's
15 declaration?

16 MS. CIPRIANO: Objection to the
17 extent it calls for privileged information.

18 You can answer the question "yes" or
19 "no" if you remember.

20 A. I don't recall the specific order in
21 which things were provided to me.

22 BY MR. HOAGLAND-HANSON:

1 Q. You did receive Dr. Matz's
2 declaration?

3 A. I did.

4 Q. It was already drafted, right?

5 A. Yes.

6 Q. Your declaration relates to work
7 that you did at the University of Texas, right?

8 A. That's right.

9 Q. Did you review any of your documents
10 from Texas when you were preparing your
11 declaration?

12 A. Which documents do you mean? I
13 reviewed this manuscript, which was from Texas.
14 I don't believe there were any other documents I
15 was asked to review from Texas.

16 Q. You didn't review laboratory
17 notebooks from Texas?

18 A. No. That's correct. As in many
19 labs, the way it works in the Matz lab is that
20 laboratory notebooks remain with the laboratory.
21 So my laboratory notebooks from that work remain
22 in Dr. Matz's laboratory.

1 Q. Did you review any other documents
2 from Texas, other than the manuscript itself?

3 A. No, I haven't.

4 Q. Did you get UT's permission before
5 testifying in this case?

6 A. Did not ask. Was never advised that
7 that was a permission that I had to seek.

8 Q. Does -- so UT doesn't know that
9 you're testifying about your work?

10 A. I could only speculate. I don't
11 know.

12 Q. Do you think that any of your
13 testimony in this case relates to anything that's
14 confidential to Texas?

15 A. No, I don't.

16 Q. Is it fair to say that everything
17 that you're testifying about is based on what was
18 publicly available in your manuscript?

19 A. I think I'm testifying based on what
20 was publicly available in the manuscript as well
21 as my own memory of the process that we used to
22 produce that manuscript.

1 Q. Do you think you're revealing any
2 confidential information from the University of
3 Texas by doing that?

4 A. I do not.

5 Q. Why not?

6 A. I'm not sure what information in
7 this paper could be considered confidential
8 information of -- that belongs to the University
9 of Texas. All of this information was entered
10 into public -- into the public record, either as
11 a published paper or data uploaded to public
12 archives.

13 Q. When you were working at the
14 University of Texas as a postdoc, did you have an
15 agreement that any intellectual property you
16 generated as a result of your work belonged to
17 Texas?

18 MS. CIPRIANO: Objection. Scope.

19 A. I don't recall signing any such
20 document. There often are intellectual property
21 agreements between faculty members and
22 universities, but I don't recall any such

1 agreement as a postdoc.

2 BY MR. HOAGLAND-HANSON:

3 Q. Was it your understanding that you
4 were free to use work that you did in the lab at
5 UT for your own personal use?

6 MS. CIPRIANO: Objection. Scope.

7 A. I guess I'm -- I'm uncertain what
8 you mean by "personal use." What I am doing here
9 is discussing in public with -- discussing in
10 public the -- the paper that I've written and
11 published. So I -- I have -- I have no concerns
12 that I'm disclosing any -- any secrets by doing
13 that.

14 BY MR. HOAGLAND-HANSON:

15 Q. Dr. Meyer, I'm going to hand you
16 what's been previously marked as Patent Owner's
17 Exhibit 2101.

18 (Whereupon, Patent Owner's Exhibit
19 2101, Redline of Eli Meyer declaration, was
20 identified.)

21 BY MR. HOAGLAND-HANSON:

22 Q. Dr. Meyer, this is a redline of your

1 declaration that was provided to us -- well, that
2 was filed by your lawyers in this case that shows
3 the changes between your declaration and
4 Dr. Matz's declaration; is that right?

5 A. That's right.

6 Q. And so this -- this redline reflects
7 the changes that you made to what Dr. Matz had
8 written, right?

9 A. This reflects the changes that I and
10 counsel together have made.

11 Q. Let's start with paragraph 1.
12 There's an insertion here. You say, "I
13 understand that Dr. Mikhail Matz previously
14 submitted a declaration at Ex2039."

15 Do you see that?

16 A. I do.

17 Q. And what's your basis for that
18 understanding?

19 A. That's what was communicated to me
20 by counsel.

21 Q. And I think you already said this,
22 but just so the record's clear, you never spoke

1 with Dr. Matz about your declaration, right?

2 A. That's correct.

3 Q. A few lines down, you say, "I have
4 independently verified the content and analyses
5 that Dr. Matz included in his declaration."

6 Do you see that?

7 A. I do.

8 Q. What does that mean?

9 A. It means that I reviewed his
10 declaration, evaluated whether I agreed with it
11 or whether I felt that any changes needed to be
12 made to it, and found that I agreed with the
13 substance of all the opinions that he expressed
14 in the declaration, and I had only minor phrasing
15 changes to make for purposes of clarification.

16 Q. So it's fair to say that if you
17 didn't edit it, you agree with it, right?

18 A. That's fair.

19 Q. How did you verify your declaration?

20 MS. CIPRIANO: Objection to form.

21 A. The -- the term "verified" here is
22 intended to reflect that I reviewed it and

1 confirmed that I believe it's correct.

2 BY MR. HOAGLAND-HANSON:

3 Q. Did you look at any documents as
4 part of the verification process?

5 A. I reviewed the documents that we've
6 discussed here.

7 Q. Which documents do you mean?

8 A. The manuscript itself and the
9 supplementary information attached to the
10 manuscript and the declaration itself, these were
11 the primary resources for evaluating whether I
12 felt that the declaration was a -- a fair and
13 accurate summary of the manuscript.

14 Q. You didn't look at any other
15 documents?

16 A. I don't recall looking at any
17 documents beyond the ones that we've listed here.

18 Q. You don't have any reason to think
19 that Dr. Matz looked at any other documents in
20 preparing the original version of the
21 declaration, right?

22 MS. CIPRIANO: Objection.

1 Speculation.

2 A. I could only speculate about his
3 process for producing the original declaration.
4 He and I never discussed that process, and I
5 never saw any of the previous versions. I only
6 saw his version of the declaration that was
7 conveyed to me by counsel.

8 BY MR. HOAGLAND-HANSON:

9 Q. Dr. Matz is still at UT, right?

10 A. That's right.

11 Q. Do you know if he has the original
12 laboratory notebooks relating to this work?

13 MS. CIPRIANO: Objection.

14 Speculation. Scope.

15 A. I can't be certain. I can say that
16 I think the -- his general practice, as in most
17 labs, is to keep those laboratory notebooks more
18 or less indefinitely. So I would guess he has
19 them, but I'm -- I'm guessing.

20 BY MR. HOAGLAND-HANSON:

21 Q. Do you think Dr. Matz has access to
22 the original sequencing data that was created as

1 part of this manuscript?

2 MS. CIPRIANO: Same objections.

3 A. Actually, I can answer that one
4 firmly. Everyone has access to the original data
5 because they were uploaded to the public sequence
6 archive.

7 BY MR. HOAGLAND-HANSON:

8 Q. Do you think Dr. Matz has any other
9 sequence information other than what was uploaded
10 to the sequence archive?

11 MS. CIPRIANO: Objection.

12 Speculation. Scope.

13 A. I don't know. I don't know what
14 other sequence data he has kept.

15 BY MR. HOAGLAND-HANSON:

16 Q. Okay. Then you say, "I confirm that
17 I have reached the same independent opinions on
18 this matter."

19 A. Yes.

20 Q. How did you go about reaching
21 independent opinions on this matter?

22 A. I evaluated whether I agreed with

1 his opinion. Yeah, I'm not sure what to add to
2 that.

3 Q. It's -- it's fair to say that you
4 started from the Matz declaration and not from
5 your manuscript, right?

6 A. That's -- that's a fair statement.
7 I was evaluating whether I thought the
8 declaration was a fair and accurate summary of
9 the manuscript. So that process would have
10 involved looking at the declaration and then
11 looking at the manuscript and evaluating is that
12 an accurate summary.

13 Q. You say, "My testimony only concerns
14 my opinions and the public materials in the Meyer
15 publication."

16 Do you see that?

17 A. I do.

18 Q. How are your opinions different from
19 what the publication says?

20 MS. CIPRIANO: Objection. Misstates
21 the record.

22 A. Well, my opinions often include

1 statements that aren't explicitly included in the
2 manuscript itself such as the context of why we
3 chose to do something a particular way.

4 BY MR. HOAGLAND-HANSON:

5 Q. Anything else other than why you
6 chose to do things?

7 A. I suppose there are details of the
8 process that may not be explicitly included in
9 the manuscript, for example, our previous
10 discussion of where did this 2200 number come
11 from.

12 Q. If you go ahead to paragraph 3,
13 Dr. Meyer, it says, "Tecan requested that I
14 submit this declaration to aid the Patent Office
15 in its review of Meyer."

16 You see that?

17 A. I do.

18 Q. What does that mean?

19 A. I took that to mean that the -- I
20 intended that this refers to the counsel for
21 Tecan rather than any individuals at that company
22 in itself.

1 Q. What exactly did Tecan ask you to
2 do?

3 MS. CIPRIANO: Objection to the
4 extent it calls for privileged information.
5 You can answer at a high level.

6 A. It was requested that I review this
7 declaration and evaluate whether I agreed with it
8 and edit where I felt it was necessary.

9 BY MR. HOAGLAND-HANSON:

10 Q. Did -- what's your understanding of
11 what this proceeding is about?

12 A. I have a very -- very little
13 understanding of what this hearing is about. I
14 understand that it relates to a dispute over a
15 patent, but I have not even evaluated what patent
16 or patents those may be, so I -- I have very
17 little -- very little knowledge about the overall
18 case.

19 Q. You have not reviewed the patents
20 that are at issue in this proceeding?

21 A. Correct. I have not.

22 Q. You haven't reviewed any of the

1 other expert reports that have been submitted?

2 A. Correct. I have not.

3 Q. You haven't reviewed the petition
4 that was filed at the patent office?

5 A. I have not.

6 Q. And you haven't reviewed Tecan's
7 response to that petition?

8 A. No, I have not.

9 Q. Are you aware that Tecan is seeking
10 hundreds of millions of dollars of as a result of
11 this patent?

12 MS. CIPRIANO: Objection to form.
13 Speculation and scope.

14 A. The information you've just given is
15 information I have never heard before, and I am
16 sure there's a lot of information like that
17 because I have very little knowledge of the
18 overall case.

19 BY MR. HOAGLAND-HANSON:

20 Q. Why didn't you ask about why you
21 were being ask to testify under penalty of
22 perjury in a legal proceeding?

1 MS. CIPRIANO: Objection to form.

2 A. I expressed that I don't know much
3 about this case, and we discussed the fact that I
4 don't know much about this case and concluded
5 that that was appropriate for my role in the
6 case, that that was acceptable.

7 BY MR. HOAGLAND-HANSON:

8 Q. What do you understand your role in
9 the case to be?

10 A. My understanding is that I am here
11 to provide expert opinion about the paper that I
12 wrote, about the study that I conducted.

13 Q. How do you think your declaration
14 will aid the patent office in deciding this
15 matter?

16 MS. CIPRIANO: Objection. Calls for
17 speculation.

18 A. Knowing so little about the case, I
19 can't even speculate very well. I imagine -- I
20 speculate that the information we're discussing
21 in my paper is relevant in some way to the patent
22 dispute, but I don't know any of the details that

1 may be relevant to the patent dispute.

2 BY MR. HOAGLAND-HANSON:

3 Q. Do you think that the patent office
4 can't understand your paper without your
5 declaration?

6 MS. CIPRIANO: Objection. Calls for
7 speculation. Scope.

8 A. I'm -- I'm quite new to this -- this
9 process. It's outside of my experience, but I --
10 it's my understanding that the patent office
11 often calls in expert witnesses with experience
12 in various fields to get their opinions on
13 technical matters, so it didn't seem unusual that
14 I would be called as one of those witnesses.

15 BY MR. HOAGLAND-HANSON:

16 Q. Do you think your paper was unclear
17 in some way that you are clarifying?

18 A. Generally, any time I review one of
19 my published papers years after writing it, I
20 often find ways that I would phrased things
21 differently. I think that's probably universal
22 among other authors. I don't see any -- any

1 flaws in the paper that would, you know -- any
2 major problems or anything that, but perhaps, I
3 could clarify some phrasing, and that's what I
4 see my role here as. Not that the paper was
5 wrong or unclear, but that I could expand on some
6 of the statements that were perhaps concise in
7 the paper.

8 BY MR. HOAGLAND-HANSON:

9 Q. Do you have any relationship with
10 Tecan outside of this case?

11 A. No, I don't.

12 Q. Have you ever used any of their
13 products?

14 MS. CIPRIANO: Objection. Scope.

15 A. I'm not aware of having used any of
16 their products. I know that often, there are
17 relationships among biotechnology companies such
18 that one company is bought by another, and
19 perhaps I've have used a product by one of those
20 others, but I'm not aware of having ever used a
21 Tecan product.

22 BY MR. HOAGLAND-HANSON:

1 Q. Are you familiar with a company
2 called NuGen?

3 A. The name rings a bell, but I
4 couldn't tell you anything about them.

5 Q. Do you recall using their products?

6 A. I don't recall using their products.

7 Q. Are you familiar with a company
8 called Qiagen?

9 A. Qiagen, yes.

10 Q. What about Integrated DNA
11 Technologies?

12 A. Yes.

13 Q. Would it surprise you to learn that
14 Dr. Matz consulted with us before he consulted
15 with Tecan?

16 MS. CIPRIANO: Objection. Scope.

17 A. It wouldn't surprise me. I don't
18 know what Dr. Matz has been up to for the last
19 decade or so, but I know that he has interacted
20 with various biotechnology companies, so it
21 wouldn't surprise me to learn that he had
22 interacted with a legal team representing a

1 biotechnology company.

2 BY MR. HOAGLAND-HANSON:

3 Q. Do you consider Dr. Matz a
4 trustworthy person?

5 A. I do, yes.

6 Q. You mentioned earlier that you
7 understand that you're offering opinions as an
8 expert witness; is that right?

9 A. Correct.

10 Q. What legal standards did you apply
11 in offering your expert opinions in this case?

12 MS. CIPRIANO: Objection. Form.

13 A. I am not sure what you mean by that.
14 Could you clarify "legal standards"?

15 BY MR. HOAGLAND-HANSON:

16 Q. Did your lawyers provide you with
17 any legal instructions to apply when giving your
18 opinions in this case?

19 MS. CIPRIANO: So objection to the
20 extent it calls for privileged information.

21 You can answer "yes" or "no."

22 A. Can I hear the question again to

1 evaluate the "yes" or "no"?

2 BY MR. HOAGLAND-HANSON:

3 Q. Did your lawyers provide you with
4 any legal instructions to apply when giving your
5 expert opinions in this case?

6 A. Any legal instructions? Apologies,
7 but could you clarify what you mean by "legal
8 instructions"?

9 Q. Did they tell you what legal
10 standard to apply?

11 MS. CIPRIANO: The same caution.

12 A. If I can only answer "yes" or "no"
13 to the question, I am unsure of what to answer.

14 BY MR. HOAGLAND-HANSON:

15 Q. Are you familiar with a legal
16 concept called "the person of ordinary skill in
17 the art"?

18 A. I have heard that.

19 Q. What does that mean to you?

20 A. Undoubtedly, I won't give a perfect
21 legal definition for this, but it's my
22 understanding that it refers to a sort of

1 fictional construct, like a reasonable person.

2 It refers to our expectation of what the typical
3 practitioner in this field would understand.

4 Q. Did you provide any opinions about
5 what the person of the ordinary skill should be
6 for purposes of this matter?

7 A. I don't think I've have provided any
8 statements along those lines.

9 Q. How would you go about determining
10 what qualifications the person of ordinary skill
11 should have?

12 MS. CIPRIANO: Objection. Calls for
13 legal conclusion. Scope.

14 A. So as someone unfamiliar with the
15 legal procedures, I'm just not an expert in -- in
16 that question. I could give you how I would
17 interpret it, how I would define it, but it may
18 very well differ from a real legal definition.

19 BY MR. HOAGLAND-HANSON:

20 Q. Do you understand your opinions in
21 your declaration to be offered from the
22 perspective of the person of ordinary skill?

1 A. I understand them to be offered from
2 the perspective of an expert and intended to be
3 understandable, comprehensible by a person of
4 ordinary skill.

5 Q. Are you familiar with the legal
6 concept of anticipation?

7 A. I am not.

8 Q. Did your lawyers give you any
9 instructions on the law of anticipation in
10 offering your opinions in this case?

11 A. I don't recall any discussion of
12 that term.

13 Q. Did your lawyers -- are you familiar
14 with the legal concept of obviousness?

15 A. I am obviously familiar with the
16 term, but not -- not a formal legal standard that
17 emerges from it.

18 Q. Did your lawyers give you any
19 instructions in the law of obviousness?

20 A. I don't recall any conversations
21 about that, no.

22 Q. In paragraph 4 of your declaration,

1 you say, "I understand that there are two inter
2 partes review proceedings concerning my work and
3 that IDT relies on my work for its anticipation
4 and obviousness arguments."

5 Do you see that?

6 A. I do.

7 Q. Were you curious what those
8 arguments were?

9 A. I have experienced curiousness about
10 the entire -- "curiosity" would be the word. I
11 have experienced curiosity about this entire
12 process and have restrained from asking for a
13 full explanation of every detail.

14 I certainly agree that this --
15 this -- this sentence raises the arguments that
16 you mentioned and I could have asked that
17 question, but I have not -- I have not asked
18 every question that came to my mind.

19 Q. Didn't you want to have the full
20 context of what's going on in this case before
21 you authored a bunch of opinions under penalty of
22 perjury?

1 A. It was my understanding that I'll be
2 asked opinion -- I'll be asked to give my opinion
3 in a very defined scope that is restricted to the
4 manuscript I wrote and the declaration that
5 summarizes it.

6 And it's my understanding that if I
7 expand that scope now, I could be liable for
8 questions on -- on other subjects. And I -- I
9 wasn't looking to expand the scope because that
10 would be more work for me. I restrained myself
11 to doing what was asked of me rather than asking
12 for more reviewing to do.

13 Q. So you don't really understand
14 what's going on here. You're just answering
15 questions that your lawyers posed to you?

16 MS. CIPRIANO: Objection to form.

17 A. I do not -- I do not know anything
18 about the case overall. I'm specifically here to
19 talk about my paper and the summary of the paper.
20 BY MR. HOAGLAND-HANSON:

21 Q. So you say, "I have not been asked
22 to provide any opinions as to the ultimate issues

1 of anticipation and obviousness that IDT has
2 raised."

3 Do you see that?

4 A. I do.

5 Q. Why?

6 MS. CIPRIANO: Objection to form.
7 Speculation.

8 A. This -- this sounds like a question
9 that your team may wish to ask this team.
10 It's -- the statement is simply as written. I
11 haven't been asked.

12 BY MR. HOAGLAND-HANSON:

13 Q. Do you think you are not qualified
14 to offer opinions on the issues in this case?

15 MS. CIPRIANO: Objection to form.

16 A. I think I'm qualified to offer
17 opinions within the scope that I've just
18 discussed, the paper that I wrote and the summary
19 of it. Since I don't know the information
20 outside of that scope, I can't really evaluate
21 whether I would be qualified. All I can say is,
22 I haven't been asked.

1 BY MR. HOAGLAND-HANSON:

2 Q. You consider yourself an expert in
3 NGS library preparation, right?

4 A. I do.

5 Q. And you also consider yourself an
6 expert in the development of new library
7 preparation techniques for NGS, right?

8 A. I do.

9 Q. Have you ever have any conversations
10 with Tecan's other expert in this case,
11 Dr. Bustamante?

12 A. No, I haven't.

13 Q. Have you ever met Dr. Bustamante?

14 A. I haven't. I'm not sure who that
15 is.

16 Q. In paragraph 7 of your report of
17 your declaration, towards the bottom of first
18 page, you say, "My research" -- oh, sorry. Hang
19 on.

20 The sentence before that, you say,
21 "During my academic career," you say, "I have
22 published 41 peer-reviewed papers using DNA

1 sequencing to study non-model organisms like
2 corals."

3 A. Yes, I see that.

4 Q. What does that mean?

5 A. Are you asking about the "non-model
6 organisms part"? You asked, "What does that
7 mean?" I'm just clarifying which piece you're
8 looking at.

9 Q. Yes, that's a fair question.

10 Do all 41 of your papers relate to
11 DNA sequencing?

12 A. I see your question.

13 No, no. I think we could point to
14 papers in my publication list that did not
15 involve DNA sequencing.

16 Q. So it's not entirely accurate that
17 you have published 41 papers about DNA
18 sequencing?

19 A. I think this could be a question of
20 the phrasing being imperfect. I have published
21 41 peer-reviewed papers. Not all of those
22 specifically use DNA sequencing.

1 So now that you bring up the
2 sentence, I may -- you know, if I were to rewrite
3 it, I may rephrase to clarify that point.

4 Q. Some of which use DNA sequencing?

5 A. Yes. And I -- I think it's probably
6 fair to say the majority, but -- but not every
7 single one.

8 Q. Okay. And now, maybe on the second
9 half of this, what is a non-model organism?

10 A. Yeah. So model organisms are very
11 well-studied organisms, for example, the fruit
12 fly, the laboratory mouse. These are organisms
13 that typically have a very large amount of
14 genetic resources available for them.

15 In contrast, most organisms on the
16 planet are not model organisms. They have not
17 been subjected to that level of study. And so
18 resources like genetic sequence data are not
19 available for those organisms.

20 Q. Do you have an understanding of
21 whether your research relates to what is
22 described and claimed in Tecan's patents?

1 MS. CIPRIANO: Objection to form.

2 A. I don't -- I don't know anything
3 about Tecan's patents, so I could only speculate.
4 It seems -- since I've been called here to
5 testify about this work, it seems that someone
6 must see a connection between them, but I could
7 only speculate who sees that connection and what
8 that connection would be.

9 BY MR. HOAGLAND-HANSON:

10 Q. Are you familiar with a research
11 technique called anchored PCR?

12 A. I'm not. No, I can't recall coming
13 across that.

14 Q. Do you recall ever reading a paper
15 from 1995, in "Nucleic Acids Research" by
16 Siebert, et al.?

17 A. I'd have to have more information to
18 say if I recall that. The -- the name seems
19 familiar, but I can't -- I can't retrieve
20 anything just from that.

21 Q. I am going to hand you a document
22 that was previously marked as Petitioner's

1 Exhibit 1007.

2 (Whereupon, Petitioner's Exhibit
3 1007, "An improved PCR method for walking in
4 unclaimed genomic DNA", was identified.)

5 BY MR. HOAGLAND-HANSON:

6 Q. Do you recognize this manuscript,
7 Dr. Meyer?

8 A. I don't recognize the manuscript.

9 Q. It talks about a technique called
10 "genome walking."

11 MS. CIPRIANO: Objection.

12 Foundation. Scope.

13 BY MR. HOAGLAND-HANSON:

14 Q. Do you see that?

15 A. I'm looking for the term "genome
16 walking" and not seeing it.

17 Q. Sure. Just the title of the paper,
18 it says, "An improved PCR method for walking in
19 unclaimed genomic DNA."

20 Do you see that?

21 A. Walking, okay.

22 I do.

1 Q. Do you know genome walking is?

2 MS. CIPRIANO: Objection. Scope.

3 A. I don't know.

4 BY MR. HOAGLAND-HANSON:

5 Q. The authors here, they're affiliated
6 with a group at -- a company called Clontech
7 Laboratories?

8 A. I see that.

9 Q. Are you familiar with Clontech
10 Laboratories?

11 A. I am.

12 Q. And who are Clontech Laboratories?

13 A. This is a biotechnology company that
14 I -- I believe I've used a product from at some
15 point in my research career. In fact, perhaps --
16 is the SMART cDNA synthesis kit from Clontech?

17 In any case, yeah, I'm familiar with
18 them as a biotechnology company that provides
19 products, and I may have even used some of them.

20 Q. There's also another institution
21 referenced here, the Shemyakin-Ovchinnikov
22 Institute of Bioorganic Chemistry --

1 A. Yes.

2 Q. -- at the Russian Academy of
3 Sciences?

4 A. Right.

5 Q. Do you know if Dr. Matz has any
6 affiliation with that organization?

7 A. So --

8 MS. CIPRIANO: Objection. Calls for
9 speculation.

10 A. So I don't recognize --

11 MS. CIPRIANO: Go ahead. Go ahead.

12 THE WITNESS: Okay.

13 A. I don't -- I don't recognize the
14 institute name itself, but the author last names,
15 Lukyanov, I believe that Dr. Matz was affiliated
16 with one or more of -- of those authors. I
17 recall that name, Lukyanov.

18 BY MR. HOAGLAND-HANSON:

19 Q. If you look at figure 1 on the first
20 page -- are you with me?

21 A. I am.

22 Q. There's a depiction of something --

1 an illustration of the suppression PCR effect.

2 Do you see that?

3 A. I do.

4 Q. And there are some hairpins there.

5 Do you see that?

6 A. I do.

7 Q. The -- you talked earlier about
8 hairpinning as one of the techniques in the
9 library preparation method in your 2009
10 manuscript.

11 Do you recall that?

12 A. Yeah, I think I've referred to it as
13 "PCR suppression," and "the formation of hairpin
14 structures." I recall that.

15 Q. Okay. And here it's called "the
16 illustration of the suppression PCR effect."

17 Do you see that?

18 A. I do.

19 Q. Who proposed the library preparation
20 method in -- in your Meyer 2009 manuscript?

21 A. Uh-huh. So this was a -- this was a
22 collaborative project between Dr. Matz and

1 myself. I was a new postdoc just out of graduate
2 school, and I came to his lab because of his
3 expertise in library preparation methods for
4 next-gen sequencing.

5 So this project was one of those
6 examples where he was teaching me methods of
7 next-generation library preparation.

8 So this -- this phenomenon, the PCR
9 suppression effect, was a part of his general
10 knowledge that he conveyed to me and we used in
11 this protocol.

12 Q. Do you know whether Dr. Matz got the
13 idea for the library preparation method from this
14 manuscript?

15 MS. CIPRIANO: Objection. Scope.
16 Speculation.

17 A. I -- I don't know the origin of the
18 -- the various ideas incorporated in our -- in
19 our library preparation method. It was an
20 iterative process, but I -- I certainly did not
21 invent the -- the concept, the PCR suppression
22 effect. I know that that was a part of his

1 general knowledge that -- that he trained me in.

2 MS. CIPRIANO: Kevin, if you're
3 going to switch gears, can we take a quick
4 break?

5 MR. HOAGLAND-HANSON: I -- do you
6 want take a break now, Dr. Meyer? I have a
7 few more questions, but...

8 THE WITNESS: If you have a
9 preference, I'm flexible.

10 MS. CIPRIANO: I -- I can go a
11 couple of more minutes, just need a bio
12 break.

13 MR. HOAGLAND-HANSON: Maybe just two
14 more on this reference?

15 THE WITNESS: Sure.

16 BY MR. HOAGLAND-HANSON:

17 Q. Would you characterize your library
18 preparation method as applying the technique of
19 anchored PCR?

20 MS. CIPRIANO: Objection.
21 Foundation.

22 A. So since I hadn't -- since I'm not

1 familiar with the term "anchored PCR," I wouldn't
2 have described it that way. Perhaps I'm familiar
3 with the concept under some different term, but I
4 wouldn't have phrased it that way because it's
5 not a phrase that's sort of in my vocabulary.

6 BY MR. HOAGLAND-HANSON:

7 Q. Are you familiar with the concept of
8 a "target-specific primer"?

9 A. Yes.

10 Q. What's a target-specific primer?

11 A. So target-specific primers are
12 primers that anneal to the -- the region of
13 interest rather than annealing to other regions.
14 An ideal target-specific primer would anneal only
15 to that region.

16 Q. Does your library preparation method
17 include a target-specific primer for the poly-A
18 tail?

19 A. That -- that question seems to --
20 you know, it kind of gets into semantics. So
21 I'll expand on that.

22 If you had a pair of target-specific

1 primers to amplify a particular gene, they would
2 be -- those primers would anneal and amplify one
3 specific region in the genome that is just that
4 gene, and so very clearly, that would reflect a
5 target-specific primer pair.

6 In the case of targeting the poly-A
7 tail, it's unclear that that should be referred
8 to as target specific because it's not one
9 target, it's really an entire class of molecules.

10 So perhaps, we should call it class
11 specific or something like that instead of target
12 specific.

13 Q. In your mind, is target specific
14 synonymous with gene specific?

15 A. No, not necessarily. There -- there
16 can certainly be other parts of the genome that
17 one is interested in that are not genes and that
18 you would, nevertheless, target with primers.

19 Q. Can you have a target-specific
20 primer to a synthetic sequence?

21 A. Sure.

22 Q. Like it's possible to insert via

1 various biochemical methods unknown sequence into
2 a cell's genome with DNA, right?

3 MS. CIPRIANO: Objection to form.

4 A. That's fair. There are methods for
5 doing that.

6 BY MR. HOAGLAND-HANSON:

7 Q. And then you can target those
8 insertion sites by targeting the artificial
9 sequence, right?

10 A. Yeah, this is -- this is outside my
11 personal experience, but that does match my
12 understanding of what's possible.

13 Q. Those are target-specific primers
14 then, right?

15 A. Yeah. So, again, I'd say if it's
16 targeting one particular region, then I think
17 it's very clearly target-specific. I think if
18 it's targeting multiple regions of a class, then
19 there may -- may be debate about whether "target
20 specific" is the right term; but if it's one
21 target, sure.

22 Q. Okay. Why don't we take that break.

1 MS. CIPRIANO: Thanks.

2 (Whereupon, a brief recess was
3 taken.)

4 BY MR. HOAGLAND-HANSON:

5 Q. Dr. Meyer, I want to go back to
6 Exhibit 2101, the redline of your declaration.

7 A. Okay.

8 Q. Do you have that in front of you?

9 A. I do.

10 Q. Okay. Could we look at
11 paragraph 11.

12 A. Okay. I'm there.

13 Q. In the last sentence, you say, "I
14 worked closely with all of them" -- meaning your
15 co-authors -- "and had personal knowledge of
16 their work and our disclosure of this work in
17 Meyer."

18 Do you see that?

19 A. I do.

20 Q. What parts of your declaration are
21 based on the disclosure of your work in Meyer and
22 which parts are based on your personal knowledge?

1 MS. CIPRIANO: Objection. Form.

2 A. I'm -- I'm thinking about your
3 question. I am trying to understand that
4 distinction.

5 Is your question about
6 distinguishing between personal knowledge,
7 meaning something that was not present in the
8 manuscript versus disclosure of this work in
9 Meyer, would be something that was present in the
10 manuscript?

11 BY MR. HOAGLAND-HANSON:

12 Q. I'm just asking you why you drew a
13 distinction between personal knowledge of their
14 work versus disclosure of the work in Meyer.

15 A. So I suppose my -- my goal in this
16 sentence was to emphasis that, you know, this was
17 a collaborative project with -- with multiple
18 parts, and that I did not conduct each one of
19 those parts with my own hands, but knew about
20 their work, and that this work was a part of our
21 manuscript.

22 Perhaps my phrasing of the sentence

1 could be criticized, but yeah, that was the goal
2 of my statement was that their work wasn't done
3 in secret without my knowledge, but rather, was
4 part of this open collaboration, and I have
5 knowledge of it.

6 Q. It would've been odd if your
7 co-authors had been conducting research in
8 secret, wouldn't it?

9 A. That certainly would have been odd,
10 yeah. So the -- the statement is intended to say
11 that this didn't -- this study didn't proceed in
12 an odd way. It proceeded in kind of the normal
13 way where were an open team of collaborators and
14 knew what each other were doing.

15 Q. "Personal knowledge" is an
16 interesting turn of phrase.

17 Is that a phrase that you would use?

18 A. Sure. It seems a common phrase,
19 yeah.

20 Q. What's "personal knowledge"?

21 A. Something I knew personally as
22 opposed to something that was written down in a

1 book and I could cite.

2 Q. Did you talk to any of your
3 co-authors in preparing your declaration?

4 A. No, I haven't.

5 Q. If you go to the next page, page 8,
6 there's a heading, Roman II, here.

7 Do you see that?

8 A. I do.

9 Q. It says, "The Study In Meyer Focused
10 On Sequencing The Entire Coral Transcriptome In
11 One Sequencing Run."

12 You see that?

13 A. Yes.

14 Q. What does that mean?

15 A. So when -- when you run a DNA
16 sequencing machine, it produces data in batches.
17 This is, you run the machine with a sample, and
18 it produces a bunch of data, hundreds of
19 thousands or even millions of reads. That --
20 that batch would be described as a sequencing
21 run.

22 And so you get a certain amount of

1 data from a sequencing run, depending on the
2 platform and various other details. And so our
3 goal here in this study was to sequence
4 effectively all the coral genes that -- all the
5 expressed coral genes, that is, the entire coral
6 transcriptome, using the data from only a single
7 batch or only a single sequencing run.

8 In contrast, you could imagine doing
9 that same project but combining data from ten
10 different sequence runs, right, and that would --
11 that would cost a lot more.

12 Q. Why does this matter?

13 A. Researchers are almost always
14 limited by funding, especially in fields like
15 marine biology. DNA sequencing costs money, and
16 so if you have to run the instrument twice, that
17 costs you twice as much as if you only have to
18 run it once.

19 So this was about efficiency,
20 getting as much useful data as you can while
21 spending -- while minimizing your -- your
22 expenses.

1 Q. And that would have been attractive
2 to other researchers at the time?

3 A. That's right. At least that was our
4 hope.

5 Q. I want to skip ahead a bit to
6 paragraph 22.

7 You say, "Our primary goal in Meyer
8 was to sequence the entire transcriptome."

9 A. That's right.

10 Q. Okay. You agree that your method of
11 sequencing was a method of sequencing only the
12 transcriptome, right?

13 A. We were certainly targeting the
14 transcriptome and analyzing the transcriptome.
15 That was -- that was the goal of the method.

16 Q. And as part of the library
17 preparation, you preferentially amplified the
18 transcriptome compared to other sequences, right?

19 A. Yes, I would say we selected for it
20 at a few levels, not just in terms of
21 amplification, but, overall, yes. We are trying
22 to focus on the transcriptome to generate

1 sequence data from the transcriptome

2 specifically.

3 Q. Are you familiar with a concept

4 called "the exome"?

5 A. Yes.

6 Q. What's the exome?

7 A. So the exome is all of the exomes in
8 the genome. The transcriptome is all of the
9 genes that are actually expressed. The exomes --
10 the exome, rather, is all of the genes that could
11 be expressed. In a given transcriptome, there
12 may be some genes that are not expressed, but the
13 exome will contain all of those genes.

14 Q. And that's because the exome refers
15 to a portion of the genomic DNA?

16 A. That's right.

17 Q. Whereas, the transcriptome refers to
18 the mRNA that's been translated from the genome
19 DNA?

20 MS. SELTZER: Transcribed.

21 A. Transcribed from the genome, yes.

22 BY MR. HOAGLAND-HANSON:

1 Q. Is it fair to say that the
2 transcriptome is a subset of the exome?

3 MS. CIPRIANO: Objection to form.

4 A. I think there are some subtleties to
5 the answer, but I am happy to go into them.

6 The transcriptome is a subset of the
7 exome in that some genes present in the exome may
8 be absent from the transcriptome, but I am not
9 answering with a definite yes because of the
10 subtlety that there are other pieces in the
11 transcriptome that are not present in the exome,
12 and that is due to the RNA processing.

13 BY MR. HOAGLAND-HANSON:

14 Q. There are other things that happen
15 as part of RNA transcription that might change
16 the sequence from what's in the genomic mRNA?

17 MS. CIPRIANO: Objection to form.

18 A. That's right. Primarily, I am
19 thinking here of the addition of the poly-A tail,
20 which is not present in the exome but is present
21 on every transcript.

22 BY MR. HOAGLAND-HANSON:

1 Q. It's fair to say that both the exome
2 and the transcriptome are subsets of the total
3 genetic material found in the organism, right?

4 MS. CIPRIANO: Objection to form.

5 A. In terms of gene content, again, I
6 agree and have to just draw your attention to
7 that same caveat that the modifications to the
8 RNA during RNA processing produce sequences that
9 are not present in the genome itself.

10 BY MR. HOAGLAND-HANSON:

11 Q. Would you characterize the method
12 that you used in your Meyer paper as a method of
13 targeted sequencing?

14 MS. CIPRIANO: Objection to form.

15 A. I don't think -- no, I wouldn't
16 phrase it that way because I think it would be --
17 it could be misinterpreted. It could be viewed
18 as misleading. Generally, if you talk about
19 targeted sequencing, it's targeting a specific
20 gene or a specific region or something like that,
21 and our method did not target a specific gene or
22 region, but rather, the entire class of

1 transcripts.

2 BY MR. HOAGLAND-HANSON:

3 Q. And if I said I had a method that
4 could be used to sequence the entire exome, you
5 would say that's not a targeted method of
6 sequencing?

7 A. I wouldn't -- I wouldn't describe it
8 as a targeted method because I would fear that
9 that could be misinterpreted by the reader for
10 the reasons I just stated, that it's not
11 targeting a single gene or region, and I think
12 that's how "targeted" is most commonly used.

13 Q. Your next sentence in paragraph 22
14 says, "This meant that our biggest challenge
15 would be to avoid the preferential sequencing of
16 certain genes or transcript regions."

17 Do you see that?

18 A. I do.

19 Q. And did you provided that in bold
20 and italics?

21 A. Yes.

22 Q. Why emphasize that?

1 A. There are many challenges in
2 transcriptome sequencing, and from a quantitative
3 perspective, this is one of the biggest
4 challenges. There are some genes expressed at
5 levels perhaps a thousand-fold higher than other
6 genes.

7 And so that will lead to
8 preferential sequencing of that very highly
9 expressed gene that could consume or use up the
10 great majority of the sequencing data from a
11 sequencing run. Because they are expressed at
12 such high levels, most of the DNA reads come from
13 those genes.

14 And so I am explaining this to say
15 what I mean by quantitatively. This was one of
16 the biggest challenges that most of your
17 sequencing data would go to those highly
18 expressed genes, so you preferentially sequence
19 the highly expressed genes.

20 So that's the reason for the
21 emphasis is that the quantitative importance of
22 this -- this challenge.

1 Q. Why bold and italics?

2 A. This is a stylistic choice. It's
3 somewhat arbitrary. I am not aware of any, you
4 know, formal rules about what statements have to
5 have bold or italics. So it was an arbitrary
6 choice to emphasize the region or the statement.

7 Q. Is it your choice to emphasize this
8 statement in particular?

9 A. I don't recall when this was added,
10 but because it's -- because it's not redlined, I
11 think this was present in the original -- the
12 Matz version of the declaration, but I certainly
13 agree with it and so I did not change it. It's,
14 as I say, quantitatively a very large challenge,
15 so it deserved emphasis.

16 I will say I tried to -- in
17 reviewing and editing the document, I tried to
18 not go in and make changes to what I viewed as
19 minor stylistic choices, like, the choice of
20 italics or bold here.

21 Q. It's fair to say that the choice to
22 emphasize this particular statement was

1 Dr. Matz's?

2 MS. CIPRIANO: Objection. Calls for
3 speculation.

4 A. I don't recall specifically where it
5 came in. I believe Dr. Matz's worked with
6 counsel to produce this declaration. So I'd have
7 speculate that Dr. Matz first hit the bold button
8 or did counsel hit the bold button. But I
9 believe it was emphasized in the Matz version of
10 the declaration that I received.

11 BY MR. HOAGLAND-HANSON:

12 Q. Is this the most important statement
13 that you make in your declaration?

14 MS. CIPRIANO: Objection to form.

15 A. I can't say I have evaluated the
16 relative importance of all of these statements.
17 I certainly think it was an important statement,
18 deserving of emphasis, but I have not done any
19 formal ranking of the importance of all those
20 statements.

21 BY MR. HOAGLAND-HANSON:

22 Q. It's the only statement in your

1 declaration in bold and italics?

2 A. Well, as I say, I see it as a
3 somewhat arbitrary stylistic choice. Perhaps in
4 a legal context like this, there are convention
5 or rules that I am not aware of, but that was my
6 view of the decision to bold and italicize that
7 statement. I saw it as not an important
8 stylistic choice. And so I didn't feel the need
9 to make any changes to it.

10 Q. You do not attribute any importance
11 to this particular statement over the other ones
12 in your declaration?

13 A. I think it's a very important
14 statement. I think it emphasizes one of the
15 biggest challenges in transcriptome sequencing,
16 but I am just saying, I don't have an opinion
17 about if we ranked the importance of all of these
18 statement, is this number 1 or number 2. I have
19 not gone through such a process.

20 Q. In the next sentence, you say, "This
21 required overcoming biases toward highly abundant
22 transcripts, the 3' ends of transcripts, and

1 shorter transcripts."

2 Do you see that?

3 A. I do.

4 Q. I want to talk about the second one
5 of those, in particular, which if you go to the
6 next page, there's a subsection B.

7 Do you see that?

8 A. I see that.

9 Q. It says "Overcoming Bias Towards 3'
10 ends of Transcripts."

11 Do you see that?

12 A. I do.

13 Q. You do not talk about this bias
14 towards 3' end of transcripts anywhere in your
15 manuscripts, do you?

16 A. That would surprise me if there's no
17 statements about it because that was certainly
18 one of the innovations in our protocol. We've
19 discussed this previously in today's meeting
20 about the broken-T chain.

21 I'd be happy to find a statement in
22 the manuscript, if you'd like.

1 Q. Sure. I think what we talked about
2 earlier was underrepresentation of the 3' ends,
3 right?

4 A. I see. You're right. That was our
5 previous discussion.

6 So I can -- I can tell you today,
7 how we overcame the bias towards the 3' ends of
8 transcripts. If you'd like, I could review the
9 manuscript to find a citation, if we've mentioned
10 that specifically in the manuscript.

11 Q. Yes. Well, before -- maybe to help
12 you out.

13 A. Yeah.

14 Q. If you look at paragraph 24 of your
15 declaration --

16 A. Okay.

17 Q. -- there is no citations to your
18 paper.

19 Do you see that? You might look up
20 at paragraph 23, you will see there is a citation
21 to Exhibit 1006.

22 A. Right.

1 Q. That's a citation to your paper?

2 A. Right.

3 Q. Right?

4 A. Yes.

5 Q. Okay. And if you look at
6 paragraph 24, there is no citations to
7 Exhibit 1106, right?

8 A. Yes.

9 MS. CIPRIANO: Objection to the
10 extent it misstates the document.

11 BY MR. HOAGLAND-HANSON:

12 Q. Okay. And in paragraph 25, there is
13 also no statement. There is no citation to
14 paragraph 1006, right?

15 MS. CIPRIANO: Same objection.

16 A. It seems to me that this is -- this
17 is cited and does explain the methods. If you'll
18 see the sentence on page 13 now, to avoid 3' --
19 so first paragraph, sixth line, "To avoid the 3'
20 over-representation...we use the SMART cDNA
21 amplification kit."

22 And that does refer to the

1 manuscript.

2 BY MR. HOAGLAND-HANSON:

3 Q. Okay. It refers to paragraph 13,
4 right?

5 A. I believe that's how this notation
6 works.

7 Q. And if you look back at
8 paragraph 24, Dr. Meyer, in the -- after the
9 first sentence, do you see the word "Id"?

10 A. I do.

11 Q. Do you know what that means?

12 A. I believe it -- it's referring to a
13 previous reference, but apologies, I don't recall
14 what the abbreviation actually stands for.

15 Q. Is that an abbreviation you have
16 used in your scientific work before?

17 A. We don't -- we don't use that
18 notation in scientific publications, but
19 understand that it's used commonly in legal
20 documents.

21 Q. And do you understand that to refer
22 back to the citation in paragraph 23 that's also

1 to page 13 of your manuscript?

2 A. I'm -- I'm unclear about the page
3 part, but I do understand it to refer to the
4 manuscript.

5 Q. Do you think that it refers to some
6 other page other than page 13?

7 A. I guess I'm uncertain whether the
8 convention is that it must apply to the same page
9 or whether it just simply applies to the entire
10 document. And that's just about my lack of
11 experience with the -- how citations are handled
12 in legal documents.

13 Q. How did you verify the citations in
14 your declaration before you signed it under
15 penalty of perjury?

16 MS. CIPRIANO: Objection to form.

17 A. This -- this seems related to the
18 previous question. I mean, my process for
19 verification was to -- to read the -- to read the
20 document, review the manuscript, and evaluate
21 whether I thought the document was a fair and
22 accurate summary of it.

1 I -- if I've some mistakes relative
2 to page number, I'm unaware of them.

3 BY MR. HOAGLAND-HANSON:

4 Q. Okay. So you would expect that
5 somewhere on page 13 of your manuscript, you
6 would find information to support your statement
7 that to avoid the 3' overrepresentation, we use
8 the SMART cDNA amplification kit from Takara?

9 A. So, again, I'm -- I'm expressing
10 uncertainty about the page issues, but I do
11 understand that that refers to the -- the
12 manuscript.

13 Q. Can you go to page 13 of
14 Exhibit 1006?

15 A. Sure.

16 Q. And you can take your time, but I'd
17 like you to point me, Dr. Meyer, to where on this
18 page you talk about overrepresentation of 3' ends
19 of transcripts.

20 A. I'm not certain that the page uses
21 the term "overrepresentation of 3' end of
22 transcripts. But certainly, our understanding of

1 the purpose for using the SMART cDNA synthesis
2 kit is that it overcame this -- this tendency.

3 Q. Is there anywhere else in your
4 manuscript that you talk about an
5 overrepresentation problem with respect to the 3'
6 end of transcripts?

7 A. I'm not certain that there is, but I
8 could -- you know, explicitly, I'm not sure that
9 we have explicitly used that term in the
10 manuscript.

11 Again, that was the purpose for our
12 use of the SMART cDNA synthesis kit. This is
13 part of the context that I'm trying to add today,
14 you know, the -- the purpose for choosing the
15 steps that we -- that we chose. And that was --
16 that was certainly one of the reasons for using
17 this.

18 Q. Okay. You would agree that you
19 expressly told the scientific community in your
20 paper that there was an issue with
21 underrepresentation of 3' ends, but you don't
22 anywhere tell the scientific community expressly

1 that there is a problem with the
2 overrepresentation of the 3' ends, right?

3 MS. CIPRIANO: Objection to form.

4 A. I'm uncertain that we've used the
5 phrase "overrepresentation of 3' ends"
6 explicitly. We have explicitly recommended using
7 the SMART cDNA synthesis kit, which overcomes
8 that problem. But I'm not certain that we have
9 explicitly stated that reason for it.

10 BY MR. HOAGLAND-HANSON:

11 Q. That reason for it comes only from
12 the declaration that Dr. Matz wrote in this case,
13 right?

14 MS. CIPRIANO: Objection to form.

15 A. Oh, I wouldn't say it comes only
16 from the declaration. I would say it was part
17 of -- part of our knowledge collectively for why
18 we this, why we made the choice at the time.

19 In other words, I didn't learn about
20 it for the first time when I read his version of
21 the declaration. Rather, it was our
22 understanding that that was why we were doing

1 this at the time.

2 BY MR. HOAGLAND-HANSON:

3 Q. Do you think that your
4 understanding, to the extent it's not expressed
5 in your paper, is somehow legally relevant to
6 this proceeding?

7 MS. CIPRIANO: Objection. Form.
8 Scope. Calls for a legal conclusion.

9 A. I -- I have little enough experience
10 with legal proceedings that I wouldn't express
11 opinions about -- I would hesitate to express
12 opinions about them.

13 BY MR. HOAGLAND-HANSON:

14 Q. Suffice it to say, though, this
15 section that we looked at in your declaration,
16 paragraphs 24 and 25, these paragraphs are based
17 on your understanding of what the purpose of the
18 experiment was and not based on the paper, right?

19 MS. CIPRIANO: Objection to form.

20 A. I mean, I would say these are based
21 on both the paper and my understanding. The
22 declaration attempts to add context and expand on

1 the details that are present in the paper.

2 BY MR. HOAGLAND-HANSON:

3 Q. So where in your paper do you
4 expressly or not expressly talk about overcoming
5 a bias towards 3' ends of transcripts?

6 A. Yeah. When we -- when we say that
7 we used the SMART cDNA synthesis kit, this was a
8 part of the motivation for using the SMART cDNA
9 synthesis kit. So it may be fair to say that
10 that term is not explicitly written out in the
11 manuscript, but it was part of our knowledge and
12 motivation for using that -- method. And we've
13 listed the method that we used.

14 Q. You don't talk about that motivation
15 anywhere in your manuscript.

16 A. I'm sorry. Is that -- are you
17 looking for a confirmation of that statement?

18 Q. You don't talk about the motivation
19 for using the SMART cDNA kit that you just talked
20 about with me and that's in paragraph 24 and 25
21 of your manuscript, anywhere in your paper,
22 right? Oh, sorry, just so the record is clear.

1 You don't talk about the motivation
2 for using the SMART cDNA kit that you just
3 testified about and that you discuss in
4 paragraphs 24 and 25 of your declaration,
5 anywhere in Exhibit 1006, your 2009 paper, right?

6 MS. CIPRIANO: Objection to form.

7 A. You're asking me whether I
8 explicitly refer to that motivation in the paper?

9 BY MR. HOAGLAND-HANSON:

10 Q. Yes.

11 A. I don't recall that specific
12 phrasing being in the paper. I -- and I'll say
13 again that I believe it's implied in the use of
14 the SMART cDNA synthesis kit. But if -- if one
15 wants to criticize our phrasing in the paper and
16 say that we should have expanded on that
17 motivation more, I could -- I could imagine that
18 being a fair criticism.

19 Q. How does your statement that you use
20 this kit -- how does your statement that you use
21 this kit imply a motivation to overcome
22 overrepresentation of the 3' ends?

1 MS. CIPRIANO: Objection to form.

2 A. Someone who understands this --
3 these library preparation protocols and how the
4 SMART cDNA synthesis kit works would have already
5 been familiar with these challenges and the fact
6 that it was a challenge that's resolved by the
7 use of the SMART cDNA synthesis kit.

8 So, you know, someone -- someone who
9 had read how the SMART cDNA synthesis kit works
10 would have understood that benefit.

11 BY MR. HOAGLAND-HANSON:

12 Q. Right. Well, once the -- once
13 someone in the field knows that you're using the
14 SMART cDNA kit, you're no longer concerned about
15 overrepresentation of the 3' ends, right?

16 MS. CIPRIANO: Objection to form.

17 A. I'd say someone with expertise in
18 the field would understand that using that kit
19 addresses that challenge effectively.

20 BY MR. HOAGLAND-HANSON:

21 Q. I want to go ahead to paragraph 27.
22 There's -- you've reproduced here figure 1 of

1 your paper.

2 A. Correct.

3 Q. And this is an accurate
4 representation of one of the versions of your
5 method that you describe on the paper, right?

6 A. Yes, I believe this is a accurate
7 copy of exactly the figure shown in the
8 manuscript.

9 Q. And if you go down to the -- to the
10 amplification step, right?

11 A. Yep.

12 Q. You've got red and yellow sequences
13 here, right?

14 A. Correct.

15 Q. And those correspond to adapters
16 that are eventually going to get used by the 454,
17 right?

18 A. Correct.

19 Q. And you've got two partial duplex
20 adapters that get ligated prior to the step,
21 right?

22 A. Correct.

1 Q. One's the yellow one, and one's the
2 red one?

3 A. Right.

4 Q. And you also add the yellow adaptor
5 to some sequences using a tailed primer. That's
6 the blue and yellow primer?

7 A. Correct.

8 Q. If you omit the yellow partial
9 duplex adapter from this reaction, will you
10 amplify only the 3' end?

11 MS. CIPRIANO: Objection. Form.

12 A. That's not -- not something I recall
13 ever seeing data from. I could speculate about
14 how that would behave, but I don't think I have
15 any data to base that on.

16 Would you like me to speculate?

17 BY MR. HOAGLAND-HANSON:

18 Q. Well, how would you expect that to
19 work based on your expertise in NGS library
20 preparation?

21 A. It's not a -- it's not a situation
22 that I've considered before, so I would want to

1 take a few minutes and -- and think about it.

2 It...

3 Q. Take your time.

4 A. It would be based on -- yeah.

5 Q. Okay.

6 A. So the situation -- the hypothetical
7 situation you're asking me to consider is that --
8 I'm clarifying here.

9 You're asking what would happen if
10 we only use the -- the red, the B partial, and --

11 Q. Yeah, B partial duplex, and the same
12 tailed primer.

13 A. And -- and we leave off the -- we --
14 we omit the A --

15 Q. Partial duplex.

16 A. -- partial duplex. Yeah.

17 Q. What's the product of that reaction?

18 A. And then you're asking what's the
19 product of the PCR reaction or the product of the
20 ligation reaction?

21 Q. You can take it step-wise.

22 A. Okay. So at the ligation -- at the

1 ligation reaction, we've only -- in your
2 hypothetical, we've only added a single type of
3 partial duplex adaptor so that that's only duplex
4 adaptor that's available.

5 It would ligate to the 3' end of the
6 5' fragment, the 5' end of 3' fragment, and both
7 ends of the internal fragments.

8 So those would be the products of
9 the ligation reaction. Would you like to talk
10 about the products of the PCR?

11 Q. Yeah. What are the products of the
12 amplification reaction?

13 A. Okay. And what primers are we going
14 to include in this hypothetical PCR?

15 Q. Just for simplicity, let's include
16 all of them.

17 A. Okay. So in that case, the B
18 primers, the yellow primers, will have no primer
19 binding site to anneal to.

20 So those products, the internal
21 fragments will not be produced. It looks like
22 the other products, I think, would be produced.

1 I'm sorry. That may have not been clear
2 verbally, so the internal -- the internal
3 products -- PCR products of the internal
4 fragments, I believe, should not be produced in
5 that situation, but the PCR products of the end
6 fragments, I think, would be produced.

7 Q. Right. So you would end up with
8 just the 5' and 3' end fragments, but all the
9 internal fragments would not be produced.

10 MS. CIPRIANO: Objection to form.

11 A. I think that's accurate. I should
12 give the caveat that the -- the PCR products
13 shown on the very bottom of the diagram with the
14 red region on both ends, those primers are still
15 in solution, and those primer binding sites are
16 present, so they would be produced but suppressed
17 through PCR suppression. So there may be a tiny
18 amount of them produced.

19 I'm trying to be absolutely precise
20 in answering your question. I don't think that's
21 terribly important. Yeah, that's my evaluation
22 of that hypothetical.

1 Again, we haven't done it, but I
2 think that -- I think that that is accurate, that
3 the end products could still be produced.

4 BY MR. HOAGLAND-HANSON:

5 Q. Someone with skill in NGS library
6 preparation could easily make that adjustment if
7 the goal was to only amplify the 5' and 3' ends,
8 right?

9 MS. CIPRIANO: Objection. Scope.

10 A. I think they could easily propose
11 the idea that -- that we've just discussed in
12 this conversation. Whether there may be other
13 subtleties that come up during development of
14 that method, I -- I can't speculate, but I think
15 the idea is reasonable enough.

16 BY MR. HOAGLAND-HANSON:

17 Q. So leaving the hypothetical and
18 going back to the method as drawn.

19 A. Uh-huh.

20 Q. And I think we've -- you know, we've
21 already been talking about it this way, but
22 there's 5' end fragments, internal fragments, and

1 3' end fragments, right?

2 A. Correct.

3 Q. When you -- those -- those fragments
4 refer to fragments of the original cDNAs, right?

5 A. That's right.

6 Q. And the -- the cDNAs are generated
7 by the cap kit, right?

8 MS. CIPRIANO: Objection to form.

9 A. The SMART cDNA synthesis kit is used
10 to produce those -- is used to produce the cDNA
11 molecules, and then those cDNA molecules are
12 fragmented through sonication. I'm -- I'm
13 answering in detail to say that the SMART cDNA
14 synthesis kit itself does not produce the
15 fragments.

16 BY MR. HOAGLAND-HANSON:

17 Q. Okay. Right. Yeah, and sorry. So
18 you would call this the SMART kit, not the cap
19 kit.

20 Have you ever heard it called the
21 "cap kit"?

22 A. I don't recall.

1 Q. Okay.

2 A. No, I don't. I -- I don't think
3 I've ever heard that.

4 Q. Okay. I'll call -- I'll try to call
5 the SMART kit.

6 A. Okay.

7 Q. The -- the SMART kit -- so the --
8 the way you have the -- the diagram shown here,
9 the SMART kit puts those blue cap sequences on
10 either end, right?

11 A. Yes, the -- the SMART kit is used to
12 make the first string cDNA, and that first string
13 cDNA contains the cap, the blue sequence on both
14 ends.

15 Q. And that blue sequence in this
16 application of the method is blocked from
17 ligation?

18 A. Yes.

19 Q. And it's blocked from ligation based
20 on a modification of the final nucleotide in the
21 cap sequence?

22 A. It's -- it's based on the absence of

1 a phosphate group on the end. So the natural
2 DNA, when it's fragmented, will contain those
3 phosphate groups, but these synthetic primers
4 will not so that's the mechanism.

5 Q. The fragmentation process that's
6 happening here is -- is stochastic in how it
7 fragments the strands of cDNA, right?

8 A. Yes. To expand on that, it's -- we
9 consider it random with regard to the position
10 along the fragment or along the transcript, where
11 it will break and with regard to the -- the
12 sequence content of that position.

13 Q. And it's -- similarly, the ligation
14 reaction is random in the sense that there's no
15 -- there's nothing putting a thumb on the scale
16 of which adaptor ligates it at which available
17 double strand, right?

18 A. That's right. The two adaptors
19 could ligate to either end as long as that end
20 contains the suitable phosphate groups.

21 Q. After that fragmentation step, there
22 was an end repair reaction performed, too, right?

1 A. After fragmentation, before
2 ligation. I think that's correct, but I'd want
3 to double-check the method section to make sure
4 we have the order correct.

5 So your statement was sonication and
6 then end repair?

7 Q. Yeah. So if you go to page 13 of
8 Exhibit 1006, right-hand column, first full
9 paragraph.

10 Are you with me?

11 A. I see it, yeah.

12 Q. It says, "First, the fragmented cDNA
13 was 'polished' using Klenow and T4 DNA
14 polymerases to fill in single-strand overhangs
15 that might remain after sonication."

16 A. Yes. So I agree with your
17 statement. End repair happens after sonication,
18 yes.

19 Q. And during sonication, there's
20 nothing that prevents fragmentation within the
21 blue cap sequence, right?

22 A. Correct.

1 Q. And if such a fragment is created,
2 it's then end repaired and available for
3 ligation, correct?

4 A. Correct. It should be.

5 Q. So while they're not drawn here, you
6 could also end up with fragments that are sort of
7 red or yellow adaptor, piece of the blue adaptor,
8 orange adaptor, white adaptor, red or yellow
9 adaptor?

10 MS. CIPRIANO: Objection to form.

11 A. I believe that's correct.

12 BY MR. HOAGLAND-HANSON:

13 Q. And we've talked about this a few
14 times already, but the internal fragments or the
15 external fragments that end up with yellow yellow
16 or red red, the same adaptor on both ends --

17 A. Right.

18 Q. -- those are the fragments that are
19 suppressed?

20 A. Correct.

21 Q. Your method doesn't somehow
22 distinguish by sequence suppressed fragments from

1 amplified fragments, right?

2 MS. CIPRIANO: Objection to form.

3 A. Are you asking whether given the
4 final data, looking at an individual read, are we
5 able to tell whether that read came from a
6 suppressed or amplified fragment?

7 BY MR. HOAGLAND-HANSON:

8 Q. Do you observe the suppressed
9 fragments in the sequencing?

10 A. So the suppression in principle is a
11 quantitative suppression, not a 100 percent
12 effective elimination of those molecules. Those
13 molecules can still be present in the mixture.
14 However, if you think about the DNA sequencing
15 technology and recognize that it has to have one
16 of them on one end and the other one on other end
17 in order to even be sequenced, I would not expect
18 to find them in the final pool of sequence data.
19 But if we are thinking about the intermediate
20 steps such as the pool of fragments, they could
21 be present at some level -- some low level in
22 that pool.

1 Q. Right. In other words, that, like,
2 if you're imagining the PCR reaction, you can
3 have some hairpin suppressed fragments floating
4 around still. You don't separate them out?

5 A. That's right. It doesn't eliminate
6 them or degrade them or anything like that. It
7 simply fails to amplified them.

8 Q. Right. Because it blocks the PCR
9 primers from binding?

10 A. Correct.

11 Q. But those suppressed fragments, I
12 think you just said can't be -- can't show up in
13 the sequence data because they can't be sequenced
14 by the 454, right?

15 A. Yeah, in principle, based on my
16 understanding of how the instrument works, I
17 don't see how they could be -- how they could
18 make through to the end. Perhaps there's some --
19 some inefficiencies in that process that I am
20 unaware of, but my expectation is they should not
21 make it into the sequence data.

22 Q. So it's fair to say that what makes

1 it into the sequencing data are the fragments
2 that are, by chance, ended up with the red and
3 the yellow adaptors, but not the rest of the
4 sample, right?

5 A. I think that's reasonable, yes.

6 Q. If you go to paragraph 33 of
7 Exhibit 2101.

8 Are you with me, Dr. Meyer?

9 A. I am.

10 Q. You state here, "Figure 1 is an
11 accurate representation of cDNA synthesis and
12 library preparation in the method."

13 And then you reproduce it again --
14 the same figure?

15 A. Yes, I see that.

16 Q. What do you mean by it being an
17 accurate? Sorry. Let me try a complete sentence
18 in English.

19 What do you mean by it being an
20 accurate representation?

21 A. It reflects how it really works.
22 There's a word we didn't use here that I will

1 emphasis which is "complete." We didn't say it's
2 a complete representation, but an accurate
3 representation, I would stand by. It does
4 reflect how it really works, our understanding of
5 how the process really works.

6 Q. Okay. And so we have talked a
7 little bit about the steps here. There is the
8 SMART kit. Then there is fragmentation, and I
9 take your point that there are some other steps
10 that might be omitted here.

11 A. Correct.

12 Q. So let me start over. It sounds
13 like what you were saying is this some of steps,
14 say, some of the important steps, but it's not
15 all of the steps, right?

16 A. It's not all of the steps. And I
17 would say it focuses on the innovations that we
18 introduced in the study. So just beginning at
19 the very top, we start with the RNA molecule, and
20 we don't tell you anything about how we extract
21 it or purify that RNA molecule because those were
22 not innovations we developed. So it's -- it's

1 intended to accurately reflect the innovations we
2 developed. Some of the standard methods are not
3 shown in the diagram.

4 Q. Okay. The steps that are in the
5 diagram, there's the cDNA synthesis and
6 amplification. That's the SMART kit?

7 A. Right.

8 Q. There's fragmentation by sonication?

9 A. Yes.

10 Q. That's adaptor ligation?

11 A. Yes.

12 Q. And this is PCR amplification,
13 right?

14 A. Right.

15 Q. Is there a single primer extension
16 step in this reaction?

17 MS. CIPRIANO: Objection. Form.

18 A. A single primer extension step,
19 could you clarify of what you mean by that?

20 BY MR. HOAGLAND-HANSON:

21 Q. Are you familiar with the concept of
22 a single primer extension reaction?

1 A. I have not heard someone discuss a
2 single primer extension reaction in those terms.
3 I could, you know, understand the words in it and
4 understand how a person could describe a reaction
5 in that way, but I don't recall ever hearing
6 anyone use the term "single primer extension
7 reaction."

8 Q. How do you understand that?

9 MS. CIPRIANO: Objection.

10 Foundation.

11 A. So hearing this term for the first
12 time, single primer would mean there's only a
13 single type of primer in the reaction.
14 Extension, surely refers to the extension step of
15 the polymerase chain reaction, and so I would
16 interpret that phrase to mean a reaction that has
17 a DNA template, a single primer type, and a DNA
18 polymerase. This would allow extension of that
19 partially double-stranded molecule.

20 The primer would bind to the
21 template. The DNA polymerase would extend it.
22 That's how I would interpret the phrase that I've

1 just heard.

2 BY MR. HOAGLAND-HANSON:

3 Q. Is it possible to have an extension
4 reaction that's not part of PCR?

5 MS. CIPRIANO: Objection to form.

6 A. Sure. Polymerase chain reaction is
7 a process that's typically done -- it's always
8 done in multiple steps. Multiple cycles, they're
9 referred to as. And it would be possible to do
10 that same reaction in only a single step, and you
11 wouldn't really call it PCR at that point. It
12 would simply be extension with a DNA polymerase.

13 BY MR. HOAGLAND-HANSON:

14 Q. In other words, you could add some
15 primers and a polymerase and extend, but not
16 thermal cycle and then have another primer to
17 amplify, right?

18 A. Correct.

19 Q. Is there such a reaction here?

20 A. Well, we conducted PCR in multiple
21 cycles. We never ran a single cycle and then
22 worked with the products of that single cycle.

1 But in principle, if you do PCR for, say, 15
2 cycles, you could look at theoretically that
3 first cycle as being such a reaction.

4 But, again, I'll emphasize, we
5 didn't actually do that. What that we really do
6 is mix the components together, put them in the
7 polymerase -- the thermocycler machine and wait
8 for 15 or cycles or whatever the number is.

9 Q. And you wouldn't describe the step
10 that is shown here as amplification as an
11 extension reaction?

12 A. Extension is one of the components
13 of PCR, so amplification refers to PCR, and
14 extension is one of the three steps in that, so I
15 would say it's a part of -- extension is a part
16 of amplification.

17 Q. Right. But if I amended your figure
18 to scratch out amplification, and I just wrote
19 extension, that wouldn't be scientifically
20 accurate?

21 A. Yes. I would disagree with that
22 relabeling. I think "amplification" would be

1 correct term here because what we're trying to
2 distinguish between in the figure is that some
3 products go through that exponential
4 amplification process and their products don't.
5 And that's -- that's the major distinction here.
6 I think extension wouldn't capture that
7 distinction.

8 Q. I want to go to paragraph 38 now --

9 A. Okay.

10 Q. -- of Exhibit 2101.

11 Are you with me, Dr. Meyer?

12 A. I am.

13 Q. In this section, you are talking
14 about the sonication reaction that you used.

15 Do you see that?

16 A. I do.

17 Q. And you say, "We optimized this
18 process to produce fragments there were roughly
19 300-400 nucleotides in length."

20 Do you see that?

21 A. I do.

22 Q. What does that mean?

1 A. So when you're sonicating nucleic
2 acids to fragment them, the size of your final
3 product depends on the extent of how much you've
4 broken up the initial template.

5 And you can vary that extent by
6 changing the intensity of the sonication, which
7 is sort of the -- the power of the sonicator, or
8 changing the duration, in other words, conducting
9 that process for a longer period of time.

10 Turning up the power or going for
11 longer, both of those would produce shorter
12 fragments. And so we -- we experimented with
13 this to evaluate what are the right settings to
14 produce the size range that we're looking for.

15 Q. Does that mean that is the fragment
16 size that you obtained from this particular run
17 of the experiment that you talk about in the
18 paper?

19 A. Not necessarily. That was our
20 target. I'm not sure if that's exactly the
21 number that we ended up with in the paper. And I
22 want to emphasize that any measurements that we

1 made of fragment size for the -- for this study
2 would be quite imprecise based on visual
3 evaluation of a gel in gel electrophoresis.
4 Gel -- I'm sorry. That's a hard word, huh?
5 Electrophoresis. E-L-E-C-T-R-O-P-H-O-R-E-S-I-S.

6 Q. I believe you passed the spelling
7 bee of the deposition.

8 A. That's a -- that's a long one, yeah.
9 So I'm emphasizing the lack of
10 precision in our method for evaluating the -- the
11 size range that pre -- we produced, to say that
12 if there's a slight difference in numbers between
13 the manuscript and here, I wouldn't view it as
14 important because it's a very approximate
15 estimate.

16 Q. If you go to paragraph 48 of
17 Exhibit 2101, Dr. Meyer.

18 A. I see it.

19 Q. You reproduce a figure from
20 additional file 4.

21 Do you see that?

22 A. I do.

1 Q. And there has been an additional
2 primer added to this reaction that is shown as
3 the green and yellow primer?

4 A. That's right.

5 MS. CIPRIANO: Objection to form.
6 BY MR. HOAGLAND-HANSON:

7 Q. Okay. Compared to the figure 1,
8 that process that we looked at earlier?

9 A. That's right. That green and yellow
10 primer is used in this modified protocol and not
11 used in the original.

12 Q. Okay. And that primer, you called
13 it the A+TrsaC.

14 Is that how you say that?

15 A. It's terrible, right?

16 It's A+TrsaC.

17 Q. Okay.

18 A. We had no good pronunciation.

19 Q. Okay. A+TrsaC. That primer is
20 complementary to the sequence at the let's say,
21 the end of the cap sequence?

22 MS. CIPRIANO: Objection to form.

1 A. It's hard to verbalize precisely,
2 but I'll give it a shot. It's -- it's
3 complementary to -- well, let's say the broken-T
4 chain that was introduced. It's illustrated
5 earlier in the diagram. The broken chain T
6 primer, which is introduced during first strain
7 cDNA synthesis at the 3' end of the transcript.

8 BY MR. HOAGLAND-HANSON:

9 Q. Okay.

10 A. And so the green region corresponds
11 to that or is complementary to that broken chain
12 T primer.

13 Q. And the -- you know, based on the
14 way that the SMART kit works, that that broken
15 chain T is always found at the -- directly
16 adjacent to the 3' end of the transcript?

17 A. Always. Every -- every transcript
18 has the poly-A tail, and the broken chain T
19 primer should anneal to every one of those. It's
20 possible it could also anneal to some other
21 regions if they have a sufficiently long stretch
22 of As. That's the only subtlety in my answer to

1 your question.

2 Q. Okay. And the broken chain T is an
3 artificial sequence?

4 A. Correct.

5 Q. In the sense that it's not found in
6 the cells that -- it's not found in the coral?

7 A. Right. The broken chain T primer is
8 complementary to the poly-A tail, and the poly-A
9 tail is natural. It is present in the corals.
10 The broken primer T is, going from memory, I
11 think it's 13 Cs, but it doesn't matter. It's --
12 it's a bunch of -- I'm sorry, I misspoke.

13 It's a bunch of Ts. I believe it's
14 13 Ts that are complementary to that -- that
15 region, that poly-A tail.

16 So the poly-A tail is present in the
17 corals. The broken chain T primer is
18 complementary to it, with the exception of the
19 break, the C that's introduced in the middle of
20 it is not complementary.

21 Q. Right. And you are then targeting
22 that broken chain T with this A+TrsaC primer?

1 A. Yes. That's the reason for
2 including it in the reaction is to prime off of
3 that region.

4 Q. And that broken chain T sequence is
5 not itself biologically relevant, but the
6 sequence directly upstream, downstream --

7 A. 5' of it.

8 Q. Yeah. The sequence directly 5' of
9 that is biologically relevant?

10 A. Correct.

11 Q. And, in fact, you were very
12 interested in sequencing that adjacent sequence,
13 right?

14 MS. CIPRIANO: Objection to form.

15 A. We were interested in sequencing all
16 of the regions of the transcript. That was our
17 goal, is to try to capture all the transcripts
18 and all the parts of the transcript. And that
19 includes the -- the 3' end and just upstream or
20 5' of broken chain T.

21 MS. CIPRIANO: Counsel, I don't want
22 to interrupt you, but it's 12:45. Do you

1 want to --

2 MR. HOAGLAND-HANSON: Yeah. Is this
3 a good time to break for lunch, Dr. Meyer?

4 THE WITNESS: That's fine with me.
5 (Whereupon, a luncheon recess was
6 taken.)

7 BY MR. HOAGLAND-HANSON:

8 Q. Dr. Meyer, I would like to go back
9 to Patent Owner's Exhibit 2101, the redline of
10 your declaration.

11 A. Okay.

12 Q. And I would like to go to
13 paragraph 59.

14 A. Okay. I'm there.

15 Q. Okay. And there is subsection C,
16 "SNP Validation" here.

17 Do you see that?

18 A. Yes, I see that.

19 Q. Why did you include this section in
20 your declaration?

21 MS. CIPRIANO: Objection to form.

22 A. This section expands on and adds

1 some context to the section about SNP validation
2 in the -- in the manuscript itself. I'd -- I'd
3 be happy to walk through the details of it with
4 you, but that -- I guess that was -- that was --
5 my general goal with the declaration was to
6 expand on and provide context for the study. And
7 so this was one -- one section that we included
8 in the study, and so I expanded on it here.

9 BY MR. HOAGLAND-HANSON:

10 Q. Why did you think expanding on this
11 particular section of the study was relevant?

12 MS. CIPRIANO: Objection to form.
13 Speculation.

14 A. It -- it addresses one of the
15 experimental procedures that we used. It
16 addresses a procedure that was using PCR and
17 amplifying specific targets. And so that seemed
18 like a -- that seemed relevant to the topics we
19 were discussing.

20 BY MR. HOAGLAND-HANSON:

21 Q. How so?

22 A. Well, we've been discussing the --

1 the fine points of PCR amplification and target
2 specificity. And this was another place in the
3 manuscript that used primers to amplify targets.

4 Q. You say here in paragraph 60, "We
5 used target-specific primer pairs to target and
6 enrich for each SNP."

7 Do you see that?

8 A. I do.

9 Q. What do you mean by "enrich"?

10 A. Yeah. So this project -- this part
11 of the process, our goal was validation of the
12 SNPs that we had identified in our 454 sequence
13 dataset. We were asking the question whether
14 they were real -- biologically real or just some
15 kind of error.

16 The way that we did that was to
17 develop target-specific primer pairs flanking
18 each SNP. So if the SNP is in the middle, we
19 designed primer pairs on each side of that SNP.

20 We would then -- we then amplified
21 those regions that contained the putative SNPs
22 and sequenced that pool of material using Sanger

1 sequencing.

2 So you asked what do I mean by
3 "enrich"? With that context for our process, the
4 enrichment that we're talking about is you start
5 with a DNA template, and you amplify it with
6 target-specific primer pairs. And your product,
7 the product of that PCR reaction is greatly
8 enriched for the target region you amplified,
9 relative to its initial abundance in the -- in
10 the template mixture.

11 So that's -- that's what I mean by
12 "enrich" is amplify that specific region.

13 Q. Is there a threshold of -- well, is
14 there a quantitative threshold that the amount of
15 a particular sequence needs to be increased to be
16 enriched, in your view?

17 MS. CIPRIANO: Objection to form.

18 A. I think you're asking quantitatively
19 how much would you have to increase the abundance
20 of the sequence in order for that to be fairly
21 described as enriched. Is that a fair...

22 BY MR. HOAGLAND-HANSON:

1 Q. Sure. Do you have a -- such a
2 threshold in mind?

3 A. I don't -- I don't have a number in
4 mind, no.

5 Q. If I create one more copy of the
6 sequence than would otherwise be there, have I
7 enriched for that sequence?

8 A. It seems that you could argue that
9 if you had sufficient evidence that you truly had
10 increased it by one copy number. But I think
11 that may be kind of a -- kind of an artificial
12 example to start with -- in -- in PCR like this,
13 you -- in these particular PCRs, where we were
14 amplifying the regions containing punitive SNPs,
15 we used a large number of PCR cycles.

16 And just to give you an illustration
17 of why that matters, if you use 20 PCR cycles,
18 the target should be enriched by about 1
19 million-fold.

20 So that's -- that's far -- far more
21 than the artificial example of sort of one extra
22 copy number. This was a very large enrichment,

1 quantitatively, in the -- the amount of product.

2 Q. Yeah. You know, in these reactions,
3 you have more than one set of primer pairs,
4 right?

5 A. No. Each one of these reactions was
6 a single primer pair. So a separate reaction was
7 used for up to --

8 Q. Okay.

9 A. -- to amplify and sequence each of
10 these SNPs.

11 Q. Okay. It's possible to do PCR with
12 multiple different primers, right?

13 A. That is -- that's -- that's correct.
14 People describe that as multiplex PCR. It is
15 possible, although frequently you run into
16 challenges where they interfere with each other
17 or -- the primer from one pair and the primer
18 from another pair come together to amplify a -- a
19 target you weren't intending.

20 And so because of those kind of
21 complexities, we didn't do any kind of multiplex
22 PCR. We did the typical old-fashioned

1 one-target-at-at-time PCR.

2 Q. In -- in your work with NGS
3 sequencing over the last 20 years --

4 A. Uh-huh.

5 Q. -- you're -- you've run multiplex
6 PCR reactions, right?

7 MS. CIPRIANO: Objection. Scope.

8 A. So most of our -- most of our
9 library preparation procedures -- so you -- you
10 discussed next-gen sequencing just a moment ago.
11 You said in your work with next-gen sequencing.
12 Most of our next-gen sequencing
13 library prep procedures do not use
14 target-specific primers at all. They -- they use
15 primers that are complementary to adaptors we've
16 added as in the protocol we're discussing here.
17 And so I wouldn't describe those as
18 target-specific.

19 In -- yeah, I don't -- I don't -- I
20 don't think I've ever published any studies that
21 used multiplex target-specific primers.

22 BY MR. HOAGLAND-HANSON:

1 Q. Have you ever done a multiplex PCR
2 reaction in any context?

3 MS. CIPRIANO: Objection. Scope.

4 A. I have. I mean, it's -- it's
5 outside of what we're discussing here, but in --
6 in my own work in my DNA-testing company, I've
7 experimented with multiplexing target-specific
8 primer pairs and have found exactly what I
9 described a moment ago, that it complicates
10 things, sometimes leading to amplification of
11 targets you're not interested in.

12 BY MR. HOAGLAND-HANSON:

13 Q. All right.

14 A. Yeah, so I have no published
15 examples of it, but I have experimented with it a
16 little.

17 BY MR. HOAGLAND-HANSON:

18 Q. In a multiplex PCR reaction, it's
19 possible for one set of primers to be more
20 efficient than another set, right?

21 MS. CIPRIANO: Objection.

22 Foundation.

1 A. That's true.

2 BY MR. HOAGLAND-HANSON:

3 Q. And so you might end up with more
4 copies of a particular fragment as a result of
5 that, right?

6 MS. CIPRIANO: Same objection.

7 A. I think the statement you just made
8 is true. I can't point to data or references
9 that would support it, but I think that's
10 reasonable. Different primer pairs have
11 different efficiencies.

12 BY MR. HOAGLAND-HANSON:

13 Q. If I do a multiplex PCR reaction
14 with different primer pairs, and I get more
15 fragments from one set of primer pairs than
16 another, have I enriched for that fragment?

17 MS. CIPRIANO: Objection. Scope.

18 A. I think any PCR could be described
19 as enrichment if you wanted to use it in that way
20 because you've amplified a product, you've
21 amplified a target, such that it -- it's more --
22 its relative frequency is higher in the product

1 than it was in the initial template.

2 With that said, we typically use the
3 term "enrichment" when we're talking about
4 producing libraries for DNA sequencing.

5 Typically when we're doing a standard PCR, we
6 just describe it as amplification.

7 BY MR. HOAGLAND-HANSON:

8 Q. Can we go back and look at the
9 figure that you have in paragraph 47?

10 A. Okay. I'm at paragraph 47.

11 Q. Okay. Sorry. And the -- the
12 figures below paragraph 48.

13 A. I see it.

14 Q. Okay. And in the PCR reaction here,
15 there are four primers being used?

16 A. Correct.

17 Q. There's B, A, A+halfswitch, and
18 A+TrsaC that we talked about earlier?

19 A. That's right.

20 Q. Is it possible that the A+TrsaC
21 primer is more efficient than the A or the B
22 primers?

1 A. Is it -- is it possible? Lacking
2 any information -- lacking any other information,
3 if I was presented with a diagram like this, I
4 would generally say yes, it's -- given a set of
5 primers, one of them could be more efficient than
6 another primer on the extract.

7 With that said, I can't ignore what
8 I do know about the figure, which is that the
9 primers complementary to A and B, which is to say
10 the red and yellow primers in the diagram, I
11 would expect to be the most efficient in this
12 reaction.

13 The reason is that they were
14 developed -- the sequence content of those
15 regions is specific to the 454 instrument, and so
16 these primers have been developed and optimized
17 to be very efficient.

18 In contrast, the TrsaC -- the
19 A+TrsaC primer that we're discussing in this
20 modified protocol, that hybridizes to a region
21 with a very high AT content; that is, it's
22 broken-T chain. And primers with such a sequence

1 content frequently are actually less efficient
2 than the other primers we're discussing here.

3 So, again, in general, given a set
4 of primers, I would say it's possible that one is
5 more efficient than the other; but given what I
6 know about the protocol, I don't have any reason
7 to expect that the TrsaC or halfswitch primers
8 would be the most efficient. I expect the A and
9 B primers to be the most efficient.

10 And I'm speculating here based on
11 what I -- what I understand about the protocol.
12 I haven't -- I haven't measured, for example, the
13 annealing temperatures of these primers, which
14 would be a relevant thing to -- to measure.

15 Q. It's possible that the A+halfswitch
16 and A+TrsaC primers are more efficient than the A
17 plus B.

18 You don't know?

19 A. Well, I find it unlikely, but I
20 wouldn't -- I wouldn't say it with any certainty
21 because I'd say we should -- we should measure
22 that or make that determination based on the

1 sequence content.

2 Q. I want to talk about the next
3 section of your declaration, which starts on
4 Roman -- page -- let me try again.

5 I want to go to paragraph 62 of
6 Exhibit 2101.

7 A. Okay. I'm there.

8 Q. Okay. And in this paragraph, you
9 say, "I understand that IDT's petition makes
10 representations about our study."

11 Do you see that?

12 A. I do.

13 Q. And you've edited the next sentence
14 from what Dr. Matz had originally said.

15 Do you see that?

16 A. I do.

17 Q. And why did you revise this
18 sentence?

19 A. My reading of his phrasing seemed to
20 imply -- seemed to suggest that he had seen these
21 representations made by IDT and disagreed with
22 those representations.

1 Because I have not seen those
2 representations, I wanted to make it clear in my
3 phrasing that -- I wanted to clarify that in my
4 phrasing, that I had not seen them. I didn't
5 want to suggest that in my phrasing. And so that
6 was the reason for this sort of change in tone
7 that I adopted.

8 Q. It's fair to say that your
9 statements in this section are based on the
10 characterization of IDT's positions that you
11 received from your lawyers, right?

12 MS. CIPRIANO: Objection to form.

13 A. That is the only information I have
14 about them, yes.

15 BY MR. HOAGLAND-HANSON:

16 Q. Why didn't you ask your lawyers to
17 review what IDT actually said?

18 A. As I've mentioned earlier, it did
19 occur to me fairly early in the process that
20 there was a lot of information about this
21 proceeding that I didn't have at my disposal.

22 I wasn't asked to review it, and as

1 I thought it through, it seemed that if I asked
2 to review it, that would be a lot the extra work,
3 and I was not sure what was motivation for that
4 extra work beyond curiosity.

5 Q. You didn't want to do a more
6 difficult, more comprehensive analysis?

7 MS. CIPRIANO: Objection to form.

8 A. I hadn't been asked to it, and
9 lacking experience with proceedings like this, I
10 didn't see any reason for me to ask for more
11 information.

12 BY MR. HOAGLAND-HANSON:

13 Q. In paragraph 65, you say, "I have
14 been informed by counsel for Tecan that this
15 study has been used in these proceedings to
16 suggest that the primers targeting the CAP primer
17 and broken chain T sequences (as disclosed in
18 Figure 1 and in Additional File 4) result
19 selective enrichment of the end fragments."

20 Do you see that?

21 A. Yes.

22 Q. What did you understand selective

1 enrichment in that sense to mean?

2 A. Enrichment of those end fragments
3 relative to the rest of the pool of fragments.

4 Q. Did counsel provide you any
5 instructions on what the definition of selective
6 enrichment is for purposes of these proceeding?

7 A. No. I don't recall any definition
8 being provided. I think we relied on my
9 understanding of the term.

10 Q. Would you agree with me that the
11 word "enriched" just means to process, so as to
12 add or increase the proportion of a desirable
13 ingredient?

14 MS. CIPRIANO: Objection to form.

15 A. I think a key part of the definition
16 should be relative to something. So perhaps we
17 can add that to your definition, relative to all
18 of the other ingredients or something along those
19 lines.

20 BY MR. HOAGLAND-HANSON:

21 Q. How much of an increase relative to
22 the other ingredients is required?

1 A. I am not aware of any quantitative
2 threshold that's agreed upon in terms of what
3 constitutes enrichment.

4 If the target has been enriched
5 relative to the other potential targets, even by
6 a small amount, someone could describe that as an
7 enrichment. I am not aware of any, yeah,
8 quantitative threshold for making that
9 determination.

10 Q. Do you whether your library
11 preparation method increased the number of 3'
12 fragments relative to the rest of the mRNAs, even
13 by a small amount?

14 A. I don't know. I don't know. When
15 you are asking about an increase -- a difference
16 in the level like that, you would really need to
17 have replicates to evaluate whether the relative
18 frequency of the target that you obtained in this
19 experiment is statistically more than you started
20 with.

21 And we didn't have replicates in
22 this experiment. So I -- I don't that feel that

1 we have -- I don't feel that we have the data at
2 hand to make that determination.

3 Q. You say, "Our goal was precisely the
4 opposite: to obtain data that would represent
5 all genes and all parts of all transcripts as
6 evenly as possible, without any preferences or
7 biases."

8 Do you see that?

9 A. I do.

10 Q. Do you think it matters what your
11 goal was versus what actually happened?

12 MS. CIPRIANO: Objection to form.

13 A. Do I think it matters? In -- in
14 what sense?

15 BY MR. HOAGLAND-HANSON:

16 Q. I don't know. You are saying your
17 goal was the opposite.

18 Did you achieve that goal?

19 A. Did we achieve that goal?

20 Certainly, we produced a sequence dataset that
21 included 5' ends of genes, 3' ends of genes, and
22 internal regions of genes. We produced dataset

1 that wasn't completely lacking in any one of
2 those three categories.

3 I don't -- I don't think we have the
4 data at hand to evaluate whether -- whether the
5 frequency of those fragments in the final pool
6 was more or less than it started at or more or
7 less than the other fragments. But I can say in
8 terms of presence and absence, we achieved the
9 goal in term of representing all of the regions
10 of the -- of the genes.

11 Q. Do you have an opinion one way or
12 the other as to whether the result of your
13 library preparation method is an even
14 distribution of genes and parts of transcripts?

15 MS. CIPRIANO: Objection. Scope.

16 A. Do I have an opinion of whether it's
17 an even representation of the different parts?

18 Yes. The word "even" seems to be a
19 quantitative comparison, and I -- I'm not sure on
20 the numbers that would support that conclusion.

21 Again, at the level of presence or
22 absence, my opinion is that it was successful.

1 We succeeded in producing sequence data from
2 these three different regions, but I am unsure if
3 we have the -- if we have data that we would need
4 to make that quantitative comparison that I think
5 you are asking for.

6 BY MR. HOAGLAND-HANSON:

7 Q. Would it matter what your goal was
8 if, in fact, you increased the proportion of 3'
9 end fragments, let's say?

10 MS. CIPRIANO: Objection to form.

11 A. I had the same question.

12 What do you -- what do you mean by
13 "would it matter?"

14 BY MR. HOAGLAND-HANSON:

15 Q. If you tell the world these are the
16 results of my method, but actually, my goal was
17 something else, right, does it matter to the
18 scientific community what your goal was in
19 evaluating your method?

20 MS. CIPRIANO: Objection to form.

21 A. Does it matter to the scientific
22 community? I guess in that scenario, both --

1 both statements would be interesting to the
2 scientific community, what your intention was and
3 what you actually achieved.

4 BY MR. HOAGLAND-HANSON:

5 Q. Right. But in that scenario, your
6 intentions are relevant mostly because it just
7 goes to show that you didn't do a very good job
8 of achieving your goal, right?

9 MS. CIPRIANO: Objection to form.

10 A. I suppose you could spin it either
11 way. You're presenting a case where you achieve
12 in a study something that's different than what
13 your goal was. It seems to me, both could be
14 interesting.

15 Certainly, there have been
16 scientific discoveries that were so-called
17 accidents that were not the intention of the
18 discoverer.

19 Our statement of the goal here is
20 really about describing the reasons for the
21 method that we developed. It was a method we
22 developed in order to represent all genes and all

1 parts of those genes.

2 BY MR. HOAGLAND-HANSON:

3 Q. I want to look at paragraph 67. You
4 say, "We created the broken chain T-primer solely
5 to resolve the 'poly-A blinding' problem during
6 454 sequencing."

7 Do you see that?

8 A. I do.

9 Q. "The breaking of the poly-T chain in
10 no way impacted the relative proportion of 3' end
11 fragments that were amplified during library
12 preparation."

13 Do you see that?

14 A. I do.

15 Q. What's your support for that
16 sentence?

17 A. When we're comparing two values like
18 this, our null hypothesis is that there's no
19 difference, those two values being the original
20 relative proportion of 3' end fragments and the
21 final proportion of the 3' end fragments.

22 We would require evidence to discard

1 that null hypothesis and conclude that there had
2 been a change in the relative proportion, and I
3 don't think we have evidence to support rejecting
4 that hypothesis, so we stay with the default
5 hypothesis that there's no change.

6 We see the 3' end fragments are
7 present in the final library, and we lack
8 sufficient evidence to evaluate whether they are
9 present at a higher or lower level. So we leave
10 it at that statement that we can't conclude
11 they've been impacted.

12 Q. Does this sentence that's in
13 paragraph 67 appear anywhere in your manuscript?
14 Exhibit 1006.

15 A. I am not aware of that sentence
16 occurring in the manuscript. It seems like quite
17 a specific sentence about this proceeding, so I
18 don't believe this was taken directly from the
19 manuscript.

20 Q. You talked about a null hypothesis.
21 Does that null hypothesis that you just talked
22 about appear anywhere in Exhibit 1006?

1 A. I don't think so. I am using
2 standard terms from scientific hypothesis
3 testing. I am just trying to illustrate the
4 logic of my statement here that our starting
5 point is the assumption that these two values are
6 not different and then we require evidence to
7 discard that hypothesis and conclude they are
8 different. And it's my position that we don't
9 have enough evidence to conclude that they are
10 different.

11 Q. Okay. And can you just point me
12 today, Dr. Meyer, to anywhere in Exhibit 1006
13 where you say that the relative proportion of 3'
14 end fragments was unaffected by library
15 preparation?

16 MS. CIPRIANO: Objection to form.

17 A. That it was -- that the relative
18 proportion was unaffected by library preparation?
19 I -- I don't recall that statement appearing in
20 the manuscript. We generally don't make explicit
21 statements that something hasn't changed.

22 You generally reserve those

1 statements for when you can demonstrate that
2 there's been a change. Certainly, the manuscript
3 demonstrates that we produced them, but the
4 relative proportion of them, we discuss it in the
5 discussion, but we certainly don't conclude that
6 it's -- that the relative proportion has been
7 increased. That's -- that's not the conclusion
8 that we state in the paper.

9 BY MR. HOAGLAND-HANSON:

10 Q. So I want to go back to that because
11 I understand you to be talking about the sentence
12 that we talked about earlier on page 9 of
13 Exhibit 1006.

14 A. That's correct.

15 Q. Right. And just so the record is
16 clear, what you said in your paper at the time is
17 that the broken-T was found in slightly more than
18 the expectation of reads, right?

19 A. Slightly -- yes, slightly more than
20 the expectation of 10 percent.

21 Q. Okay. And you didn't say this
22 demonstrated that our library preparation in no

1 way impacted the relative proportion of 3' end
2 fragments?

3 A. I mean, we -- we didn't make that
4 negative statement that it did not impact them.
5 The following sentence really states our
6 conclusion, which is that the 3' ends were well
7 represented in our dataset.

8 Remember that the challenge we were
9 dealing with here was the underrepresentation of
10 3' ends. And so if we get enough 3' ends in the
11 dataset, that demonstrates that we've overcome
12 that -- that underrepresentation.

13 So simply that they were well
14 represented, that was -- that was our big
15 conclusion about the 3' ends. They are well
16 represented in the -- in the library.

17 Q. Okay. Isn't it perfectly logical to
18 interpret this as saying, you expected to get
19 less 3' ends. You got more 3' ends, and so you
20 overshot it a bit.

21 MS. CIPRIANO: Objection to form.

22 A. So those two numbers are certainly

1 different, right? 16 percent is more than
2 10 percent. The question is whether -- whether
3 that's a statistically significant difference
4 that we can be confident about the statement that
5 the observed frequency is greater than the
6 expected frequency.

7 And I think, as we've been
8 discussing, there's -- there's reasons -- there's
9 reasons that we cannot use these data to draw
10 that -- or to support that conclusion.

11 BY MR. HOAGLAND-HANSON:

12 Q. Right. You keep saying the word
13 "confident."

14 Do you understand that it's somehow
15 legally required that we be confident that
16 something happened or didn't happen?

17 MS. CIPRIANO: Objection to form.

18 A. So as I've said, my -- my
19 understanding of these legal proceedings is
20 limited, but I'm familiar with the scientific
21 publication process. And the scientific
22 publication process involves peer review by

1 critical readers. And those readers, those
2 reviewers, pay special attention to any
3 differences that you claim.

4 So if you claim that this value is
5 higher or lower than this other value, they will
6 look critically at the data that you're using to
7 draw that conclusion.

8 Because we did not have enough data
9 to make that confident determination that one
10 value was higher than the other, we don't draw
11 that conclusion. We drew the conclusion that the
12 3' ends are well represented, that we've
13 effectively overcome the underrepresentation
14 problem.

15 BY MR. HOAGLAND-HANSON:

16 Q. And you also draw the conclusion
17 that you observe slightly more than your
18 expectation, right?

19 A. The 16 percent value is slightly more
20 than the 10 percent value, yes.

21 Q. And none of the editors or reviewers
22 of this paper said, I have reason to think that

1 your numbers on page 9 are a bit dubious. Can
2 you tell me if they're statistically significant?

3 A. That -- that was never brought up in
4 review. But I'll again draw your attention to
5 the conclusion that we actually stated. We did
6 not state that they had been enriched. We simply
7 stated that they were well represented.

8 And I think reviewer -- the
9 reviewers and editors considered our data
10 sufficient to support our conclusion. If we had
11 tried to present a different conclusion, I
12 suspect they would have been more critical of the
13 data that we were using.

14 Q. Did your lawyers tell you that
15 according to them, every single one of the
16 chemistry steps that they claim in their patent
17 happens if you perform your library preparation
18 method accord to additional file 4?

19 MS. CIPRIANO: Objection to form.

20 And to the extent it calls for
21 privileged information, you can answer "yes"
22 or "no."

1 A. For a "yes" or "no" answer, can I

2 hear the answer again, please?

3 BY MR. HOAGLAND-HANSON:

4 Q. Sure.

5 Did your lawyers tell you that
6 according to them, every single one of the
7 chemistry steps claimed in the patent happens if
8 you perform the library preparation method you
9 set out in additional file 4?

10 MS. CIPRIANO: Same objections.

11 A. No.

12 BY MR. HOAGLAND-HANSON:

13 Q. Do you think it's odd that
14 Dr. Bustamante doesn't say that your library
15 preparation method does not have all of the
16 chemistry steps that are required by Tecan's
17 patent claim?

18 MS. CIPRIANO: Objection.

19 Foundation.

20 A. I just -- I just lack the
21 information to evaluate. You asked if I find it
22 odd. I lack the information to evaluate that. I

1 don't know the steps in Tecan's patent, and I
2 don't know what Dr. Bustamante has said. I don't
3 even know who that is. So I -- I can't evaluate
4 whether that statement is odd.

5 BY MR. HOAGLAND-HANSON:

6 Q. If you go back to your declaration,
7 2101, and you go to paragraph 69.

8 A. Okay.

9 Q. You say, "Our library preparation
10 scheme, (Figure 1) uses CAP primer sequences as
11 anchors to strategically direct the placement of
12 454 amplification and sequencing primers (A and
13 B)."

14 Do you see that?

15 A. I do.

16 Q. Is the CAP primer -- is the CAP
17 primer primer target specific?

18 A. So the CAP primers are attached --
19 in our procedure, they're attached to all
20 expressed genes in the transcript. And so when
21 you use them for amplification, you're amplifying
22 all the expressed genes.

1 For that reason, I would hesitate to
2 describe it as target specific because I feel
3 that could be misleading into thinking we're
4 amplifying a specific region or a specific gene.

5 Q. Is the A+TrsaC primer in additional
6 file 4 a target-specific primer?

7 A. I -- I would have the same objection
8 to that phrasing. It -- it targets a region of
9 the transcript that's present on all expressed
10 genes. And so I think "target-specific" would be
11 a confusing term to use.

12 Q. Does target-specific, to you, have
13 to be gene specific?

14 A. No. As we discussed, it could be a
15 nongene region of the genome, right? It could be
16 an internal transcribed spacer. It could be any
17 number of nongene parts of the genome.

18 To me, "target-specific" is a term
19 that's best used when you're discussing an
20 individual target such as an individual gene or
21 an individual region rather than an entire class
22 of genes or regions.

1 Q. So if I have a primer that's
2 specific to some sequence for which there's a
3 high degree of homology across multiple different
4 genes, that is no longer a target-specific
5 primer?

6 A. Right. When we -- when we encounter
7 a situation like that, we say that we found a lot
8 of nonspecific primer. That's the term that
9 often comes up in those situations, that this --
10 this primer is not annealing to a specific
11 region, but rather, it's nonspecific. It's
12 annealing to many, many regions.

13 Q. But what if my intent is to amplify
14 a lot of different things?

15 A. So then, I think would be best
16 described as gene family specific or domain
17 specific or class specific, depending on what
18 that group of entities is that you're targeting.

19 But if you call it target-specific,
20 I think many readers will interpret that as
21 meaning a single target, and that's why I
22 would -- I would restrict my use of that term

1 to -- to those cases.

2 Q. Is it fair to say that if I'm
3 interested in a highly homologous sequence, then
4 in our hypothetical, I could have a sequence of
5 interest-specific primer that is not target
6 specific?

7 MS. CIPRIANO: Objection. Form.

8 A. So you're describing a
9 sequence-specific primer. You could have, for
10 example, a motif-specific primer, a motif being a
11 particular sequence region within a longer
12 sequence.

13 I -- you could develop primers that
14 are specific to any group that you're interested
15 in based on homologous sequences, like you're
16 describing, but we're discussing how would you
17 describe those, how would you label those.

18 And I'm trying to clarify that
19 unless it was an individual target, I would
20 describe it using the group name, so
21 motif-specific or domain-specific or
22 gene-family-specific, something along those

1 lines.

2 Q. In -- in your understanding,
3 target-specific primer is also a question of
4 primer design where the primer has been designed
5 so as to be specific for a single thing; is that
6 fair?

7 A. Yeah, that's fair. When you're
8 designing a primer, you want to make it specific
9 so it binds only to what you want it to bind to
10 and not the other things.

11 Q. And in your view, to be target
12 specific, the thing that is designed to bind to
13 has to be a single gene?

14 A. Yes. I think that's the -- the
15 clearest way to use the term "target specific."

16 Q. Could you have something target
17 specific to an artificial sequence?

18 A. Yes, you could.

19 Q. But it would have to be an
20 artificial sequence that only appears in a
21 defined location?

22 A. Or that -- or that only occurs once

1 regardless of location. It doesn't have been
2 location specific.

3 Q. I want to go to paragraph 74 of
4 Exhibit 2101.

5 A. Okay.

6 Q. In paragraph 74, on the first
7 sentence, you write, "As I explained above, the
8 prediction of the expected fraction of 3' end
9 fragments (10%) is an approximation, and 16% is
10 well within the limits of its uncertainty."

11 Do you see that?

12 A. I do.

13 Q. Do you provide those limits of
14 uncertainty anywhere in your paper, Exhibit 1006?

15 A. No.

16 MR. HOAGLAND-HANSON: Why don't we
17 take a quick break.

18 THE WITNESS: Okay.

19 (Whereupon, a brief recess was
20 taken.)

21 MR. HOAGLAND-HANSON: We have no
22 further questions for Dr. Meyer.

1 Thank you very much for your time.

2 MS. CIPRIANO: And I don't have any
3 questions for Dr. Meyer, so thank you.

4 COURT REPORTER: Rough and 2-day?

5 MR. HOAGLAND-HANSON: Yes.

6 MS. CIPRIANO: Rough and regular
7 delivery.

8 (Time noted: 2:22 p.m.)

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1 CERTIFICATE OF SHORTHAND REPORTER NOTARY PUBLIC

2 I, Monique Cabrera, the Officer
3 before whom the foregoing deposition was
4 taken, do hereby certify that the foregoing
5 transcript is a true and correct record of
6 the testimony given; that said testimony was
7 taken by me stenographically and thereafter/
8 reduced to typewriting under my direction;
9 and that I am neither counsel for, related
10 to, nor employed by any of the parties to
11 this case and have no interest, financial Or
12 otherwise, in its outcome.

13 IN WITNESS WHEREOF, I have hereunto
14 set my hand this 10th day of October, 2025.

15
16 
17 _____

18 MONIQUE CABRERA
19 Notary Public in and for
20 The State of New York
21 County of Suffolk
22 My Commission No. 01CA6043156
Expires: 06/12/2026

1 Case: Integrated DNA Tech., Inc. vs Tecan Genomics, Inc.

2 Witness Name: Eli Meyer, PhD

3 Deposition Date: 10/10/2025

4

5

6 Please be advised that the transcript in the above
7 referenced matter is now complete and ready for signature.

8 The deponent may come to this office to sign the transcript,
9 a copy may be purchased for the witness to review and sign,
10 or the deponent and/or counsel may waive the option of
11 signing. Please advise us of the option selected.

12 Please forward the errata sheet and the original signed
13 signature page to counsel noticing the deposition, noting the
14 applicable time period allowed for such by the governing
15 Rules of Procedure. If you have any questions, please do
16 not hesitate to call our office at (202)-232-0646.

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4 SIGNATURE PAGE

5 Case: Integrated DNA Tech., Inc. vs Tecan Genomics, Inc.

6 Witness Name: Eli Meyer, PhD

7 Deposition Date: 10/10/2025

8 I do hereby acknowledge that I have read

9 and examined the foregoing pages

10 of the transcript of my deposition and that:

11 (Check appropriate box):

12 () The same is a true, correct and

13 complete transcription of the answers given by

14 me to the questions therein recorded.

15 () Except for the changes noted in the

16 attached Errata Sheet, the same is a true,

17 correct and complete transcription of the

18 answers given by me to the questions therein

19 recorded.

20 _____
DATE

WITNESS SIGNATURE

21

22 _____
DATE

NOTARY

1 Errata Sheet

2 NAME OF CASE: Integrated DNA Tech., Inc. vs Tecan Genomics, Inc.

3 DATE OF DEPOSITION: 10/10/2025

4 NAME OF WITNESS: Eli Meyer, PhD

5 Reason Codes: 1. To clarify the record.

6 2. To conform to the facts.

7 3. To correct transcription errors.

8 Page ____ Line ____ Reason ____

9 From _____ to _____

10 Page ____ Line ____ Reason ____

11 From _____ to _____

12 Page ____ Line ____ Reason ____

13 From _____ to _____

14 Page ____ Line ____ Reason ____

15 From _____ to _____

16 Page ____ Line ____ Reason ____

17 From _____ to _____

18 Page ____ Line ____ Reason ____

19 From _____ to _____

20

21

22

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