

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

3
4 PARSE BIOSCIENCES INC.,
5 Petitioner,

6
7 v.

8
9 10X GENOMICS, INC.
10 Patent Owner.

11
12 Case IPR2023-00876
13 U.S. Patent No. 10,155,981
14

15
16 REMOTE DEPOSITION of GREGORY COOPER, Ph.D.
17 Thursday, May 2, 2024
18 9:00 a.m. CST
19

20 Job No.: 534770

21 Pages: 1 - 160

22 Reported By: Michelle M. Yohler, CSR, RMR, CRR

1 The deposition of Gregory Cooper, Ph.D., held
2 remotely pursuant to notice before Michelle M.
3 Yohler, CSR, RMR, CRR, a certified shorthand
4 reporter, CSR No. 84-4531.

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(Continued)

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E X A M I N A T I O N S

WITNESS	PAGE
GREGORY COOPER, PH.D.	
By Mr. Baughman.....	7
By Mr. Walter.....	146
By Mr. Baughman.....	156

E X H I B I T S

EXHIBITS FIRST REFERENCED (Not Attached)	PAGE
No. 1002 Declaration of Gregory Cooper, Ph.D., in Support of Petitioner for Inter Partes Review.....	9
No. 1003 Linnarsson.....	93
No. 1059 Declaration of Gregory Cooper, Ph.D., in Support of Petitioner's Reply to Patent Owner's Response.....	8
No. 1067 "Polyadenylation of mRNA in Prokaryotes".....	146

(Continued)

1	E X H I B I T S		
2	No. 1068	"RNA Polyadenylation in	
3		Prokaryotes Organelles;	
4		Different Tails Tell Different	
5		Tales".....	148
6	No. 2013	Expert Declaration of John	
7		Quackenbush, Ph.D.....	9
8	No. 2101	"Alteration of Sequence	
9		Specificity of the Type IIS	
10		Restriction Endonuclease BtsI"....	133
11	No. 2102	BMC Genomics Article "Efficient	
12		and cost-effective bacterial	
13		mRNA Sequencing from Low Input	
14		Samples Through Ribosomal RNA	
15		Depletion".....	72
16	No. 2103	Cell Article "Single-Cell	
17		Approaches in Human Microbiome	
18		Research".....	66
19			
20			
21			
22			

1 P R O C E E D I N G S

2 (Technician read-on.)

3 MS. REPORTER: Before I swear the witness
4 in, can I please have all attorneys identify
5 themselves and who they represent for the record.

6 MR. BAUGHMAN: Sure. It's Steve Baughman
7 and Josh Reich for the patent owner from
8 Groombridge, Wu.

9 MR. WALTER: Derek Walter of Weil,
10 Gotshal & Manges for Petitioner Parse.

11 (WHEREUPON, the witness was duly sworn.)

12 GREGORY COOPER, Ph.D.,
13 called as a witness herein, having been first duly
14 sworn, was examined and testified as follows:

15 EXAMINATION

16 BY MR. BAUGHMAN:

17 Q Good morning, Dr. Cooper. I know you've
18 been through this a bunch of times, so we'll skip
19 a lot of the formalities at the beginning, but I
20 want to make sure that you have access to the
21 exhibits we put in the download link.

22 A Yep. I have them.

1 Q Great.

2 And I assume that those are the only
3 things you have access to; those are clean copies
4 and you don't have notes or anything else
5 available to you; is that right?

6 A That's correct.

7 Q And just one more formality. I assume you
8 don't have any apps open that would let you see
9 messages from somebody else except us?

10 A No.

11 Q Very good.

12 Okay. Your reply declaration in this
13 proceeding is Exhibit 1059; is that correct?

14 (WHEREUPON, Exhibit No. 1059 was first
15 referenced.)

16 BY THE WITNESS:

17 A Let me -- oh, I see. Sorry. Yes.

18 BY MR. BAUGHMAN:

19 Q Feel free to go ahead and open that up.

20 A Yep.

21 Q Okay. What was your understanding of what
22 you were doing in this reply declaration?

1 MR. WALTER: Objection. Form.

2 BY THE WITNESS:

3 A So my understanding is that it's written
4 as a response to Dr. Quackenbush's report and some
5 of the arguments therein.

6 BY MR. BAUGHMAN:

7 Q And is Dr. Quackenbush's report you're
8 referring to Exhibit 2013?

9 (WHEREUPON, Exhibit No. 2013 was first
10 referenced.)

11 BY THE WITNESS:

12 A Let me -- yes, that looks correct.

13 BY MR. BAUGHMAN:

14 Q Thanks.

15 And is it your understanding that
16 Dr. Quackenbush in Exhibit 2013 was responding to
17 your original opinions in your opening
18 declaration, which is Exhibit 1002?

19 (WHEREUPON, Exhibit No. 1002 was first
20 referenced.)

21 BY THE WITNESS:

22 A So it would be my understanding that his

1 declaration would be in part a response, but it
2 could encompass other things, I suppose. But I
3 don't know the full scope of what's excepted in
4 that opening report for patent owner in an IPR.

5 BY MR. BAUGHMAN:

6 Q Is it your understanding that in your
7 reply declaration, you were allowed to change your
8 original opinions?

9 A No, I don't believe so. And I don't
10 believe I did change any of my original opinions.
11 It was more about focused and addressing specific
12 things that I had objected to or disagreed with
13 Dr. Quackenbush.

14 Q And is it your understanding that you were
15 allowed here to start over with new opinions in
16 your reply declaration?

17 A No, I don't believe there are any new
18 opinions.

19 Q Do you have an understanding about whether
20 Dr. Quackenbush will be allowed now to put in
21 another declaration responding to your reply
22 declaration?

1 A I believe patent owner has a -- what I
2 called a surreply, so I assume he is, but I'm not
3 sure about the rules of an IPR.

4 Q Did you read Parse's petition in this IPR?

5 A The original petition?

6 Q Yes.

7 A Yes.

8 Q When did you read it?

9 A Oh, I don't remember. I probably looked
10 at it multiple times, but I may have looked at it
11 early on before even agreeing. But, yeah, I can't
12 say when I was -- it may have been months ago; I
13 don't remember.

14 Q Did you read it before it was filed?

15 A I do not believe so, no.

16 Q Have you read Parse's reply paper in this
17 IPR?

18 A The same reply that was filed at the same
19 time as my reply declaration? Yes.

20 Q Did you read that before it was filed?

21 A I may have. I remember talking about it.

22 It was right around the same time it was filed. I

1 don't know -- I didn't put any substance into it,
2 so I looked at it, but it was right around the
3 same time it was filed. So it may have been a day
4 or two before, day or two after; I don't know.

5 Q Did you make any suggestions or comment on
6 the document before it was filed?

7 A No, not on the specific text of the -- I
8 mean, we had been -- it could have been indirectly
9 because we had been talking about my declaration
10 reply, so I don't know to what extent anything
11 that I was -- that I had spoken about with the
12 Weil folks in terms of my declaration, I don't
13 know if that shaped that reply brief, but I didn't
14 specifically comment on any tech aspect of the
15 reply brief.

16 Q In your declaration, you lay out the
17 elements of the patent claims that you're opining
18 about; is that right?

19 MR. WALTER: Objection --

20 BY MR. BAUGHMAN:

21 Q I'm sorry, I should say Exhibit 1002, your
22 original declaration.

1 A So in my original declaration, I did walk
2 through each sort of element of the '981 claims
3 and how Linnarsson and McCloskey and some of the
4 other evidence relates to those.

5 Q And you addressed the same claim
6 limitations again in your reply declaration,
7 correct, with the same numbering?

8 A Certainly the claim numbers are the same.
9 I don't -- I can't say that all the formatting
10 with the As and Bs translated exactly, yes, but
11 it's the same claim, same elements, yes.

12 Q Give me one second to find a page number
13 for you.

14 Can I ask you, please, to open
15 Exhibit 1002, your original report.

16 A Okay.

17 Q And look at Paragraph 195.

18 MR. WALTER: Hold up a second. The
19 documents, when you download them, they're not --

20 MR. BAUGHMAN: Certainly.

21 MR. WALTER: -- it's hard to find things.

22 MR. BAUGHMAN: And, Derek, please let me

1 know when you're ready. I don't want to go ahead
2 without you.

3 MR. WALTER: Okay.

4 BY MR. BAUGHMAN:

5 Q Are you there, Dr. Cooper, at
6 Paragraph 195 of Exhibit 1002?

7 A The paragraph that reads, "It is my
8 opinion that Linnarsson discloses a method
9 comprising"?

10 Q Yes.

11 A Yes.

12 Q I bring you here simply to show you what's
13 been numbered element 1G of the claim right above
14 it; do you see that?

15 A I do.

16 Q And I know in your reply declaration,
17 Exhibit 1059, you also talk about limitation 1G;
18 is that right?

19 A I believe so, but if you want me to look,
20 I can find the exact section.

21 Q I can give you an example. In
22 Paragraph 54 of Exhibit 1059, you refer to

1 claim 1G, correct?

2 A Yes, that looks correct.

3 Q And it requires sequencing the plurality
4 of tagged polynucleotides to obtain a plurality of
5 identified polynucleotide sequences?

6 A That's right.

7 Q In your opinion, how much of the tagged
8 polynucleotide needs to be sequenced to meet this
9 claim limitation?

10 MR. WALTER: Objection. Form.

11 BY THE WITNESS:

12 A So I don't think the claim -- the claim
13 language doesn't specify any specific portion; it
14 just says sequencing the plurality to obtain a
15 plurality of identified polynucleotide sequences.

16 So I suppose there's an implicit
17 limitation there that you have to be able to
18 identify the sequence, but there's no statement --
19 no quantitative assertion within the claim about
20 some fraction or length or whatever.

21 BY MR. BAUGHMAN:

22 Q So is it your view that part of the tag

1 has to be sequenced?

2 A Well, I would say that in this particular
3 claim element, you just have to sequence the
4 tagged polynucleotides. It doesn't say you have
5 to sequence a tag, but there are contextual
6 elements here that -- there are other parts of
7 claims that inform you that you have to use the
8 tags for certain regions, and to the extent that
9 you would need to use the tag for other
10 limitations, then obviously you would need to
11 sequence that tag.

12 Q And would that be part of the tag or all
13 of the tag?

14 MR. WALTER: Objection. Form.

15 BY THE WITNESS:

16 A You would have to sequence enough of the
17 tag to use it in compliance with the limitation
18 imposed by the other portions of the language of
19 those claim elements that talk about, for example,
20 using the first tag to differentiate cells.

21 But I don't necessarily think you have to
22 sequence the whole tag. You may -- maybe or maybe

1 not, as long as you're using it for the purpose
2 that the claim dictates.

3 BY MR. BAUGHMAN:

4 Q Would you need to sequence some of the
5 polynucleotide corresponding to the sample
6 polynucleotide?

7 A Yes, I believe that is part of -- again,
8 doing this 1G as part of a series of other steps
9 that are required by the claim, yes.

10 Q And, again, how much of that?

11 MR. WALTER: Objection.

12 BY THE WITNESS:

13 A The -- I don't see a statement in the
14 claims that narrow it to any specific quantitative
15 measure in terms of what portion it required.

16 BY MR. BAUGHMAN:

17 Q I'm going to ask you to look at
18 Exhibit 1059. That's your reply declaration,
19 please.

20 A Okay.

21 Q And I may sometimes just say your new
22 declaration or your reply declaration. If I do

1 that, I mean to refer to Exhibit 1059. Is that
2 okay with you?

3 A 1059 is the reply or -- or new?

4 Q Yes.

5 A Yeah, that's fine.

6 Q And if I ever confuse you about that, feel
7 free to ask me, and I'll try to clarify with an
8 exhibit number.

9 A Okay.

10 Q Thank you.

11 In Paragraph 29 of your reply declaration,
12 Exhibit 1059, you describe Figure 1 of Linnarsson;
13 do you see that? Paragraph 29.

14 A Yes, I see that.

15 Q And in Paragraph 29, you say, "Linnarsson
16 generally teaches this method in Figure 1
17 comprising the following steps," colon, and then
18 there's a quote and a list of steps.

19 Do you see that?

20 A I do.

21 Q In your opinion, simply by making these
22 statements about Figure 1, has Linnarsson

1 disclosed any and every way of tagging and
2 sequencing tagged polynucleotides?

3 A Any and every way? So, no, I don't -- I
4 think I would agree it says what it says, and it
5 provides a general overview of the disclosed
6 methods within Linnarsson as providing a sort of
7 summary of each individual step. I don't think
8 it's describing necessarily the entire universe of
9 all possible methods of tagging or sequencing.

10 Q Can I ask you, please, to look at
11 Paragraph 126 of your reply declaration that's
12 Exhibit 1059. Right near the end, if that helps.

13 A You said 126?

14 Q 126, please. Yes.

15 A Okay.

16 Q Do you see that in Paragraph 126 you state
17 that in your original declaration, which I
18 understand is Exhibit 1002, you, quote, undertook
19 a detailed obviousness analysis of Linnarsson and
20 McCloskey, including explanations of how they are
21 analogous and relate to the same field of endeavor
22 as the '981 patent; is that right?

1 A Yes.

2 Q Is that a true statement?

3 A I believe so.

4 Q Could I ask you, please, looking at
5 Exhibit 1002, to show me where in that original
6 declaration you explain that Linnarsson is
7 analogous to the '981 patent?

8 A So starting with the 1059 reply quotes to
9 Paragraphs 27 to 37; wherein, it describes the
10 sort of general overview of the '981 claims, and
11 it talks about how the patent generally describes
12 methods for analyzing nucleic acids from two or
13 more single cells.

14 And it also refers to Paragraphs 99 to 104
15 of the declaration that talks about a general
16 overview of McCloskey, including that it describes
17 a method of DNA analysis for single cell samples
18 that utilizes tag sequences.

19 And it also refers to Paragraphs 108 to
20 117 of the original that talk about Linnarsson in
21 general in how that teaches a method of analyzing
22 gene expression in a plurality of single cells by

1 preparing a tagged cDNA library.

2 And Paragraphs 186 to 194 as well speak to
3 this subject.

4 Q Can you point to any text in those
5 paragraphs that actually equates Linnarsson and
6 the '981 patent or connects the two of them?

7 A I think I just did. I talk about how they
8 are all focused on the same endeavor about looking
9 at single cells, tagging nucleic acids, sequencing
10 them, analyzing them, et cetera.

11 So they're clearly directed to the same
12 general topic. Same field of endeavor I think is
13 the way to put it.

14 Q Is there a statement, though, in your
15 Exhibit 1002 that says they are in the same field
16 of endeavor, the two of them?

17 A So you're asking about the 1002 now?

18 Q Your original declaration, Exhibit 1002.

19 A So in Paragraph 187, it says that the
20 Linnarsson -- the Linnarsson and McCloskey
21 references are in the same field of endeavor.

22 Q Yes, McCloskey and Linnarsson in the same

1 field of endeavor; I see that. Do you see any
2 statement that Linnarsson and the '981 patent are
3 in the same field of endeavor?

4 A So in Paragraph 185, I mention that only
5 analogous art may be considered in an obviousness
6 analysis and then provide the definition that that
7 art is analogous if it is in the same field of
8 endeavor.

9 And, again, I provide lots of scientific
10 details about why McCloskey, Linnarsson, and the
11 '981 are all transitively in the same field of
12 endeavor.

13 Q But you can't find in Exhibit 1002 any
14 statement that Linnarsson and the '981 patent are
15 in the same field of endeavor, correct?

16 MR. WALTER: Objection. Form.

17 BY THE WITNESS:

18 A So, again, I think I provided lots of
19 scientific evidence as to why they're in the same
20 field of endeavor.

21 BY MR. BAUGHMAN:

22 Q So I understand you're arguing that

1 there's a basis for saying so, but can you point
2 to any place in Exhibit 1002 where you did say so?

3 A So I just pointed out in the
4 paragraph when I talk about my understanding of
5 the rules of even conducting an obviousness
6 analysis is that they're required to be in the
7 same field of endeavor, and that, therefore, it
8 logically follows that I find the '981 and
9 Linnarsson and McCloskey to be in the same field
10 of endeavor.

11 Q So your testimony today is that in
12 Paragraph 25 where you stated your understanding
13 of the legal rules governing your analysis, that
14 statement is enough to assert that Linnarsson and
15 the '981 patent are in the same field of endeavor?

16 A I think combined with all of the
17 scientific evidence I provide that they are in the
18 same field of endeavor is sufficient, yes, I think
19 that point is clear.

20 Q And you say in your reply declaration you
21 included explanations of how they are in the same
22 field of endeavor as each other, but you did not

1 state in Exhibit 1002 that they are, correct?

2 MR. WALTER: Objection. Form.

3 BY THE WITNESS:

4 A Sorry, we're talking about 1059 or 1002
5 now?

6 BY MR. BAUGHMAN:

7 Q In 1059, you say that you gave
8 explanations of how Linnarsson and the '981 patent
9 are in the same field of endeavor, correct?

10 A That's right.

11 Q Where is that explanation saying that '981
12 and Linnarsson are in the same field of endeavor?

13 MR. WALTER: Objection. Form.

14 BY THE WITNESS:

15 A So, again, I point to Paragraphs 27 to 37,
16 99 to 104, 108 to 117, and 186 to 194 as
17 paragraphs in the 1002 that are relative to this
18 question.

19 BY MR. BAUGHMAN:

20 Q So you'll agree that in the 1002
21 declaration, you did not state that Linnarsson and
22 '981 are in the same field of endeavor?

1 MR. WALTER: Objection. Asked and
2 answered. Form.

3 BY THE WITNESS:

4 A I don't agree with that at all. I just
5 explained that the -- my understanding of the
6 rules of the obviousness analysis; I explained
7 about all the scientific analysis that places them
8 in the same field of endeavor; so, no, I disagree
9 with that statement.

10 BY MR. BAUGHMAN:

11 Q But there are no words saying that '981
12 and Linnarsson are in the same field of endeavor
13 in your Exhibit 1002?

14 MR. WALTER: Objection. Form.

15 BY THE WITNESS:

16 A Again, I disagree. What I said previously
17 is that I provide lots of evidence; I talk about
18 my understanding of the -- of the requirements to
19 do an obviousness analysis; and provide lots of
20 evidence as to why they're in the same field of
21 endeavor. So that to me is very clear from the
22 declaration.

1 BY MR. BAUGHMAN:

2 Q But you don't have a sentence saying they
3 are analogous?

4 MR. WALTER: Objection. Form. Asked and
5 answered.

6 BY THE WITNESS:

7 A I disagree with that. I think it's very
8 clear from my declaration they're in the same
9 field of endeavor.

10 BY MR. BAUGHMAN:

11 Q But you didn't state that in so many
12 words, unless you can point that to me, correct?

13 MR. WALTER: Objection. Form. Asked and
14 answered.

15 BY THE WITNESS:

16 A So, again, if you look at Paragraph 25, if
17 you look at all the paragraphs we just discussed
18 about all the scientific evidence, I feel it is
19 very clear.

20 BY MR. BAUGHMAN:

21 Q Would you agree, Dr. Cooper, that the only
22 mentions of the word "analogous" in your

1 declaration Exhibit 1002 are in Paragraph 25 where
2 you state the rules and in Paragraph 187 where you
3 equate McCloskey and Linnarsson but not the '981
4 patent?

5 A So, I guess, there's two parts of that
6 question. If you just do a search for the word
7 "analogous," it appears three times in those two
8 paragraphs that we just discussed.

9 But it's unreasonable to suggest that's
10 not about the '981 patent, considering the entire
11 declaration is focused on the claims of the '981
12 patent.

13 Q And those two paragraphs are Paragraph 25
14 and Paragraph 187 in Exhibit 1002, right?

15 A That's correct.

16 Q And you don't mention the '981 patent in
17 Paragraph 187.

18 A So, again, the whole document is focused
19 on the claims of the '981. The literal numbers
20 "'981" don't appear in those two paragraphs, but I
21 don't find that relevant to the understanding of
22 how you would read it.

1 And I should say that the -- especially
2 187, for example, talks about analysis of single
3 cells with tagging, et cetera, so there's lots of
4 shared claim language with the '981 that makes it
5 very clear.

6 Q So you could make an argument now that
7 they are analogous, but you don't set forth an
8 explicit argument in your Exhibit 1002 that they
9 were, correct?

10 MR. WALTER: Objection. Asked and
11 answered. Form.

12 BY THE WITNESS:

13 A I disagree with that. I think we've
14 already gone through why I believe it's clear from
15 my declaration that the '981 and Linnarsson and
16 McCloskey are all analogous to one another.

17 BY MR. BAUGHMAN:

18 Q Dr. Cooper, would you agree that
19 Linnarsson's method begins with releasing mRNA
20 from each cell -- each single cell to provide a
21 plurality of individual mRNA samples?

22 A Well, I -- this might be helpful to go

1 back to the Figure 1 language, I believe it starts
2 with "obtaining a sample." Would probably be a
3 better characterization of what Linnarsson starts
4 with; you have to have some input from which you
5 obtain your polynucleotides.

6 Q Would you agree that Linnarsson then
7 releases mRNA from each single cell to provide a
8 plurality of individual mRNA samples?

9 A So, yes, at some point in Linnarsson, you
10 release -- from the sample that you get, you
11 obtain single cells and then release mRNA -- or
12 release polynucleotides generally from those
13 single cells, including mRNAs.

14 Q Would you agree that in Linnarsson, the
15 mRNA is indiscriminantly released from each single
16 cell?

17 A I'm not sure I understand what you mean by
18 "indiscriminantly."

19 Q Have you ever used the phrase "the mRNA in
20 Linnarsson is indiscriminantly released from each
21 single cell"?

22 A I may have. I don't -- I can't remember

1 sitting here right now. It's possible. I
2 don't...

3 Q In your own usage, what does the word
4 "indiscriminantly" mean?

5 A Without -- sort of, without any scheme of
6 selection, just sort of randomly.

7 Q And is it your understanding that in
8 Linnarsson, the mRNA is released from each single
9 cell in the way you just used the word
10 "indiscriminantly"?

11 A Certainly it -- as a general matter,
12 there's no requirement that you do it any specific
13 way, but I don't -- what I'm trying to understand
14 is I don't know that you could not practice
15 Linnarsson with a method that did it differently,
16 but, in general, it is released. So they're
17 just -- the cells are just lysed opened and mRNA
18 is released at random or indiscriminantly.

19 Q Do you agree that Linnarsson doesn't
20 describe any additional elimination or filtration?

21 A I wouldn't make a blanket statement to
22 that effect, but I'm just sort of saying I don't

1 think the methods are necessarily incompatible
2 with that, but there are certainly embodiments
3 that -- in which the cell is open -- popped open
4 and all the mRNAs are released indiscriminantly.

5 Q Do you agree that in Linnarsson, the
6 released mRNA sample comprises substantially all
7 mRNA molecules of each single cell?

8 A I don't -- I don't think it's necessarily
9 required. I think in some embodiments, it would
10 happen that way.

11 As one example, depending on how the lysis
12 happens, there could be RNAs in the nucleus that
13 aren't released, as those in cytoplasm, et cetera.
14 So there could be ways to implement a method that
15 wouldn't necessarily include all, it would be a
16 subset.

17 Q But would you agree that Linnarsson's
18 method as you understand it did include all?

19 A Not necessarily in all embodiments. I
20 think there are methods that would fall within the
21 scope of Linnarsson's disclosure that would not
22 release all.

1 Q For all the embodiments you relied on
2 here, would you agree that it is all?

3 A No, I wouldn't agree with that because to
4 the extent that lots of the steps of Linnarsson --
5 so, for example, just priming a cDNA synthesis
6 reaction doesn't require that the input include
7 everything.

8 So I don't think Linnarsson really
9 provides any specific exclusion or inclusion of
10 that sort of statement. It can be done in
11 multi -- in a multiplicity of ways, including all,
12 including a subset, et cetera.

13 Q So you disagree with the statement that in
14 Linnarsson, because the mRNA is indiscriminantly
15 released from each single cell and because
16 Linnarsson does not describe any additional
17 elimination or filtration, the released mRNA
18 sample comprises substantially all mRNA molecules
19 of said cell?

20 A I don't think I said that.

21 Q Well, do you disagree with it?

22 A So I would reiterate my previous response

1 that there's -- that Linnarsson discloses a series
2 of general steps; that you can have elements
3 within them that provide differential performance
4 or differential behaviors.

5 Which, again, the example of cytoplasmic
6 versus nuclear RNAs, you could handle differently
7 and still practice the Linnarsson method on those
8 different kinds of -- the Linnarsson method would
9 encompass those different kinds of sample prep
10 methods.

11 So it may include all, it may not, and you
12 could still be -- and it would still be within the
13 scope of what Linnarsson describes.

14 Q Would it surprise you if you had
15 characterized Linnarsson as disclosing all?

16 A No, in the sense of at least some
17 embodiments include all, but it doesn't
18 necessarily exclude embodiments that don't include
19 all.

20 Q Would you agree that Linnarsson's method
21 then tags these sample polynucleotides for the
22 purpose of gene expression analysis?

1 A So, I mean, I think Linnarsson is
2 generally focused on gene expression, and many of
3 the elements therein are focused on gene
4 expression, yes.

5 Q Would you agree that persons of skill
6 would understand that the purpose of Linnarsson's
7 method would be to analyze substantially all mRNA
8 molecules of the cell?

9 A No, I would -- I would think that at least
10 one application of Linnarsson would include trying
11 to analyze all the mRNAs, but there are many other
12 applications of Linnarsson that would not entail
13 amplifying all mRNAs or targeting them all.

14 For example, it talks about designing
15 primers that are gene-family-specific, and so
16 there are clearly embodiments of Linnarsson that
17 only look at subsets of RNAs.

18 Q So sitting here today, you disagree that
19 persons of skill would understand that the purpose
20 of Linnarsson's method would be to analyze
21 substantially all mRNA molecules of the cell?

22 MR. WALTER: Objection. Form.

1 BY THE WITNESS:

2 A No, I don't -- what I said was that it
3 is -- Linnarsson describes a method that one might
4 use to analyze all of them, but that isn't an
5 exclusionary. It's possible to do it other -- to
6 practice methods of Linnarsson that don't look at
7 all, and it's possible to practice Linnarsson that
8 does look at all. It encompasses both kinds of
9 approaches.

10 BY MR. BAUGHMAN:

11 Q I guess I'm trying to understand your
12 answer. I'm going to try it again.

13 Dr. Cooper, do you agree that a person of
14 skill would understand that the purpose of
15 Linnarsson's method would be to analyze
16 substantially all mRNA molecules of the cell?

17 A I would state that one purpose of
18 Linnarsson is to amplify is to look at all the
19 mRNAs, but not the only purpose of Linnarsson.

20 Q So a statement that it is the purpose of
21 Linnarsson is wrong?

22 A To the extent that you're implying it's

1 the only purpose, then that's wrong, yes.

2 Q Would you agree that persons of skill
3 would understand that Linnarsson describes a
4 method which is designed to be applied to
5 substantially all mRNA molecules of a given cell?

6 A Again, but not to the exclusion of other
7 embodiments that don't look at all.

8 Q And, Dr. Cooper, you've testified about
9 Linnarsson in several different IPR proceedings
10 now; is that right?

11 A Yes. Three of them at this point, yes.

12 Q And in each case, it was the same
13 Linnarsson reference, which here is Exhibit 1003?

14 A Yes.

15 Q I'm going to ask you to look at
16 Paragraph 85 of Exhibit 1059, your reply
17 declaration.

18 A Okay.

19 Q There's a block quote there, and
20 underneath the block quote in Paragraph 85,
21 there's this statement where you say: "Thus, a
22 POSA would find it obvious from McCloskey's method

1 to expand barcodes to different lengths depending
2 on the size of a sample and needs of the
3 experiment."

4 Do you see that?

5 A I do.

6 Q And that's your testimony in your reply
7 declaration, correct?

8 A Yes.

9 Q Where in your original declaration,
10 Exhibit 1002, did you say it would have been
11 obvious from McCloskey and McCloskey's method to
12 expand barcodes to different lengths depending on
13 the size of a sample and needs of the experiment?

14 A So I think this issue is addressed
15 repeatedly in the original declaration. So, as an
16 example, if you look in Paragraph 92, I talk about
17 why -- essentially the motivation to combine
18 McCloskey and Linnarsson is to solve the
19 amplification bias problem that Linnarsson notes
20 is an issue, and, to do that, one uses the random
21 barcode strategy that is described by McCloskey.

22 And so in my original declaration, I

1 discuss at great length the nature of that
2 strategy and how it works.

3 So in Paragraph 92, for example, it says
4 that looking at the McCloskey that every sample --
5 every polynucleotide within every sample are first
6 uniquely tagged. By uniquely tagging -- and I say
7 the number of unique tags correspond to the number
8 of unique polynucleotides. So it's clear that
9 that measure of uniqueness is important.

10 I also cite to in McCloskey -- so that --
11 and that analysis appears in many places
12 throughout my original declaration.

13 I also cite specifically to the page in
14 McCloskey that defines what the random barcode is.
15 So, for example, in Paragraph 206, I talk about
16 how McCloskey has a batch stamp element and a,
17 quote, barcode to distinguish polynucleotide
18 sequences arising from different cell or allele
19 copies. And I cite to Page 763 and 764.

20 And in that 764, it provides a definition
21 of "barcode" that we just talked about, which is
22 that it's that currently a set of nucleotides, but

1 it could be a variable length, and that the
2 formula for determining how many unique barcodes
3 arise from any given length is $4n$.

4 So this is really filled throughout my
5 original declaration, both the specific definition
6 that McCloskey provides and the general nature
7 that would instruct a POSA as to how and why
8 they're using that barcode and how to incorporate
9 it into their experiment.

10 Q Where do you -- where in your declaration,
11 Exhibit 1002, do you discuss calculating the
12 number of barcodes as $4n$?

13 A Well, we just talked about Paragraph 206,
14 and I believe that's cited multiple times.

15 Paragraph 206 --

16 Q Let me stop you there before you go on to
17 other paragraphs.

18 In Paragraph 206, do you discuss
19 calculating $4n$?

20 A I cite to the specific definition that
21 McCloskey provides, which includes the $4n$
22 paragraph -- which includes the $4n$ definition for

1 the barcode.

2 Q Do you quote --

3 A (Indiscernible) in quotes for showing that
4 it's a definition and that McCloskey teaches that
5 definition.

6 Q Yeah. Do you say 4n anywhere in your
7 declaration?

8 A Again, I cite to that definition
9 repeatedly.

10 Q So it's in McCloskey, but where do you
11 cite -- where do you quote from it? Where do you
12 quote 4n?

13 A I talked about multiple locations where I
14 cite exactly to that "how the barcode is defined"
15 and point to the page number in McCloskey that
16 provides that definition which includes 4n and --

17 Q So you don't --

18 A -- context --

19 Q Sorry.

20 A Sorry.

21 This is in the context of lots of
22 explanation as to how the barcode strategy works

1 and why a POSA would want to use that randomer
2 strategy and how it would be important to go after
3 uniqueness, et cetera. So it's -- to me it's very
4 clear that that's what's written here.

5 Q And nothing in Paragraph 206 talks about
6 expanding the barcode to different lengths, does
7 it?

8 A I disagree. I talk about the nature of
9 that barcode, provide the definition, I provide
10 McCloskey's definition of it, point to the
11 citation that provides that for more detail, and
12 it's clear within the overall discussion that
13 that's what's written.

14 Q Are there any words in Paragraph 206 you
15 see that talk about expanding?

16 A Again, I refer specifically to the
17 McCloskey barcode definition which talks about how
18 the length can be variable.

19 Q So the only reference that you are
20 pointing to in Exhibit 206 about expanding
21 barcodes to different lengths depending on the
22 size of the sample and needs of the experiment is

1 your citation to page that includes the definition
2 of a barcode?

3 A Well, and, again, 206 and elsewhere I talk
4 about the nature and purpose and design strategy
5 of that barcode. And general in terms of that
6 the -- the whole point of the randomer is to get a
7 diversity of sequences.

8 So if you look at the last sentence of
9 Paragraph 206, it specifically talks about how --
10 how and why you're using that barcode and that a
11 POSA would understand that.

12 Q Do you ever use the word "length" talking
13 about a barcode in your declaration exhibit 1002?

14 A I believe I do, yes.

15 Q Where?

16 A In Paragraph 192 I talk about the lengths
17 of the Linnarsson and McCloskey barcodes and how
18 they're within -- and I provide a range for the
19 Linnarsson barcodes, for example.

20 Again, making clear that both Linnarsson
21 and McCloskey essentially contemplate variable
22 length barcodes depending on the needs of the

1 experiment.

2 Q And your statement in Paragraph 192 that
3 you just called us to is that McCloskey discloses
4 that its batch stamp typically comprises 6 to 8
5 nucleotides and its barcode comprises 7
6 nucleotides.

7 Do you see that quote from your
8 declaration?

9 A I do.

10 Q Are there any words there that talk about
11 4n or other lengths of the barcode?

12 A So, again, I cite specifically to the page
13 number that provides the definition.

14 We're talking about -- and the context
15 here of these sentences is all about
16 variable-length barcodes. It talks about
17 "typically comprises." It's -- and it's "could
18 have essentially designated."

19 So there's clearly variability
20 contemplated in both my declaration here and in
21 the documents that it's referring to.

22 Q What word in your sentence "McCloskey

1 discloses that its batch stamp typically comprises
2 6 to 8 nucleotides and its barcode comprises 7
3 nucleotides" suggests variability in the barcode?

4 A Again, the entire nature of this whole
5 sentence here we're talking about the variability
6 of lengths of barcodes in both of them; the
7 reference to the definition of the barcode, which
8 talks about the variable length of it; use of the
9 word "typically," et cetera. I feel like this is
10 very clear.

11 Q And is there any discussion in this
12 paragraph about expanding barcodes to different
13 lengths depending on the size of the sample and
14 needs of the experiment besides the citation to
15 764 in McCloskey?

16 A And the fact we're talking about the
17 Linnarsson -- the Linnarsson cell tag; the
18 McCloskey batch stamps are variable lengths and
19 how they can be combined together; and the
20 citation to 764; and the whole purpose of this
21 strategy, which is to use the McCloskey random
22 barcoding strategy to solve amplification bias.

1 Q And you state that the barcode comprises 7
2 nucleotides; those are your words, right?

3 A That phrase occurs. That phrase is
4 written there, yes, but, again, it's in the
5 context of this discussion about variable length
6 and what's typical and what a POSA can do,
7 et cetera. So it's -- it's with the citation to
8 the variable-length definition as well.

9 Q And your next sentence actually says what
10 a POSA would in your opinion do -- what you're
11 relying on a POSA to do, which is that, "A POSA
12 could have conceptually designated the first 6 to
13 8 nucleotides of Linnarsson's cell tag sequence to
14 identify the single cell origin of the tagged
15 polynucleotide and used the next 7 nucleotides to
16 distinguish the tagged polynucleotide from other
17 one of the same single cell," right?

18 A Yes, I -- I say a POSA could have done
19 that. There are a whole range of other
20 implementations that a POSA would have been well
21 empowered to do given standard competencies of a
22 person of skill in the art.

1 Q And this is in mapping to the claim,
2 right? Paragraph 192?

3 A So I think this is in the context of -- I
4 have to scroll up.

5 This is talking about motivation to
6 combine Linnarsson and McCloskey so as to render
7 obvious the claims.

8 Q And it's to render obvious element 1F,
9 right?

10 A Well, it may be used in other -- other
11 portions of the document as well, but I think the
12 motivation to mine is generally important, but
13 certainly specifically what's relevant to 1F.

14 Q And in this Paragraph 192, you don't talk
15 about other possibilities a person of skill might
16 have used, correct? You just say 7 nucleotides --
17 "its barcode comprises 7 nucleotides" in the
18 second-to-last sentence.

19 And then you say, "A POSA could have
20 conceptually designated the next 7 nucleotides to
21 distinguish the tagged polynucleotide from other
22 one of the same single cell."

1 A I'm sorry, what's the question?

2 Q You don't state in Paragraph 192 any other
3 possibility a POSA might have done in implementing
4 the combination you're arguing?

5 A Well, I believe from reading this text,
6 it's clear there's a range of possibilities. If
7 you just look at the fact that the Linnarsson
8 barcode can be up to 20, for example, and the fact
9 that we're citing to McCloskey's definition of
10 barcodes, which are themselves intrinsically
11 variable, I believe it's very clear that you can
12 tailor the length of those individual components
13 to fit the needs of your experiment --

14 Q But you agree --

15 A -- that.

16 Q Sorry.

17 You would agree, Dr. Cooper, that
18 Linnarsson discusses a range of different things.
19 You've said so.

20 A Yes.

21 Q Is it your argument that you're relying on
22 all of the different possibilities in Linnarsson

1 as your mapping for the claims here?

2 A I feel like that's a very open-ended
3 question, and I'm not comfortable answering that
4 one way or the other.

5 I talk about lots of specific evidence
6 that maps to individual claim elements, but to the
7 extent there's an argument that some claim
8 language necessarily excludes certain other
9 embodiments, I don't necessarily agree with that.

10 But, no, I'm not saying everything maps to
11 everything; I'm saying I have lots of specific
12 evidence at specific locations. But that evidence
13 of one thing doesn't necessarily preclude
14 something else from happening, I guess, is --
15 there's lots of optionality within these schemes.

16 Q And did you describe any other optionality
17 in discussing element 1F in your declaration
18 including in Paragraph 192 beyond using 7
19 nucleotides to distinguish the tagged
20 polynucleotide from other one of the same single
21 sample -- single cell?

22 A I believe we just went through this. We

1 talked about the variable-length Linnarsson; we
2 talked about the variable-length McCloskey; we
3 talked about the specific definition of the
4 barcodes that McCloskey provides on Page 764; I
5 say that they could have done this; there are
6 "typically comprises."

7 So I think it's clear that there's a range
8 of barcode lengths that one might use -- that a
9 POSA might use, and, again, design of which would
10 be totally routine and conventional practice.

11 Q So it's your testimony that in mapping
12 element 1F, to a 7-nucleotide barcode for
13 McCloskey, by using the word "could," you were
14 suggesting that there might be many other
15 possibilities that you're relying on here and that
16 patent owner and the board would need to consider?

17 MR. WALTER: Objection. Form.

18 BY THE WITNESS:

19 A I guess I would disagree. I'm giving 7 as
20 one example, and, again, talking about in the
21 context of the ranges that are implied by -- or
22 explicitly written in there, 4 to 20 in

1 Linnarsson, for example; 6 to 8 for the batch
2 stamp; and if you go to the 4n language in the
3 McCloskey citation.

4 So I think it's clear that there's a range
5 of possible limitations that all map to this claim
6 language that are expressly contemplated by a
7 combination of Linnarsson and McCloskey.

8 BY MR. BAUGHMAN:

9 Q You keep referring to the 4n language in
10 the definition, which you never quote in your
11 Exhibit 1002, right?

12 A I cite to it repeatedly.

13 Q You cite to a definition that includes
14 that and other things, correct?

15 A I cite -- I talk about, quote/unquote,
16 barcode and then provide a page number that
17 provides the full definition of barcode and -- as
18 it's used in McCloskey.

19 Q And the definition of barcode as its used
20 in McCloskey isn't limited to calculating 4n, is
21 it; it describes the function of a barcode in
22 McCloskey, correct?

1 MR. WALTER: Objection. Form.

2 BY THE WITNESS:

3 A It -- so the definition provides the
4 length of the barcode; it talks about the formula
5 for determining the diversity of barcodes that
6 account for any given length; it says that we
7 currently use 7.

8 So it clearly defines a variable scope --
9 a variable-length barcoding strategy for use in
10 reducing amplification bias.

11 BY MR. BAUGHMAN:

12 Q And you chose to state in your declaration
13 that its barcode comprises 7 nucleotides, right?

14 A That one particular sentence, it includes
15 that in the context of a section that's clearly an
16 exemplary statement.

17 Q Well, this is a section that's mapping
18 your argued combination to the claim language,
19 right?

20 A This is providing one exemplary mapping of
21 the claim of the Linnarsson and McCloskey
22 disclosures to the claim language, yes.

1 Q What other exemplary mapping do you
2 provide in this section?

3 A Again, we just talked about that, the 4 to
4 20, 6 to 8, the reference to the variable-length
5 barcode by McCloskey. It's all in there. It's in
6 the declaration that this is clearly -- that the
7 POSA could have a range of experimental design
8 choices in terms of the length of those specific
9 barcodes that would all fall within the scope of
10 what's disclosed by Linnarsson and McCloskey and
11 that map to the '981 claim, in particular this
12 step.

13 Q So apart from these last two sentences in
14 Paragraph 192, that "McCloskey's barcode comprises
15 7 nucleotides" and your statement that a person of
16 skill would use the next 7 nucleotides to
17 distinguish the tagged polynucleotide from others,
18 is there any other specific statement of ways you
19 would shape your combination to meet the
20 definition -- I'm sorry -- to meet the claim
21 limitation 1F?

22 A So I think you missed -- I don't -- I

1 didn't say they would have; I said they could
2 have. Again it suggests to me it's -- I'm giving
3 this as one example of how McCloskey and
4 Linnarsson combine to render obvious this claim
5 element in the context of a discussion about what
6 the purpose of those barcodes are, what the
7 general definition is, why you would use them, why
8 you would use particular combination.

9 And, given all that, a POSA would
10 understand that a range of barcode randomers is --
11 is essentially within the scope of design choices
12 that a POSA would use to optimize the experiment
13 for themselves.

14 Q And you didn't give any other example in
15 this section, did you, besides 7 nucleotides?

16 MR. WALTER: Objection. Form. Asked and
17 answered.

18 BY THE WITNESS:

19 A So we talked about how the Linnarsson
20 barcodes can be up to 20. So if you add -- even
21 if you have the batch stamp of 8 and the barcode
22 of 7, there's 5 extra nucleotides. So just that

1 alone suggests that you can expand that -- either
2 or both of those barcodes to the larger length.

3 So, no, I don't -- I don't agree with that
4 statement that it's the only thing written here.

5 BY MR. BAUGHMAN:

6 Q Did you specify any other example using
7 those bases or anything else?

8 MR. WALTER: Objection. Asked and
9 answered. Form.

10 BY THE WITNESS:

11 A So I -- I'm not sure I'm understanding
12 how -- we've gone through this over and over
13 again. I provide lots of definitions about how
14 the barcode is variable length, and I provide one
15 example that they could have done it with using a
16 6-to-8 batch stamp and a 7 -- 7 nucleotide random
17 barcode. I don't read that language as excluding
18 other possibilities; it's merely one example.

19 Q And, as you said, we've been talking about
20 this for a while. You have yet to point me to
21 another example where you specify what it could
22 be, correct? Another specific example with a

1 length of the nucleotides.

2 MR. WALTER: Objection. Asked and
3 answered. Form.

4 BY THE WITNESS:

5 A Yeah, I guess I didn't call out the entire
6 range of numbers that one might choose to practice
7 barcode -- to practice McCloskey. I reference the
8 fact that it's variable length as defined by
9 McCloskey. I provide the definition. I talk
10 about the purpose and how a POSA would understand
11 it. So, to me, it's very clear that it's not
12 restricted to 7.

13 BY MR. BAUGHMAN:

14 Q You said you didn't call out the entire
15 range of numbers. Did you call out any other
16 specific number besides 7?

17 A I talk about the Linnarsson barcodes are
18 4 to 20 so it would be clear --

19 Q That's not -- I'm sorry, that's not the
20 number --

21 MR. WALTER: Hold on. Hold on. Let him
22 finish. Let him finish.

1 Go ahead and finish, Dr. Cooper.

2 I wouldn't jump in like this, but you keep
3 asking the same questions over and over and over,
4 so I felt like I need to.

5 But go ahead and finish --

6 MR. BAUGHMAN: I apologize for
7 interrupting. I didn't mean to, and I'll let him
8 finish. I would --

9 MR. WALTER: Go ahead and finish. Go
10 ahead and finish.

11 MR. BAUGHMAN: Counsel, no, I'm sorry, now
12 that you started this, I would ask that you limit
13 your objections to form. Your coaching is not
14 necessary for the witness. Thank you.

15 MR. WALTER: Go ahead and finish,
16 Dr. Cooper.

17 BY THE WITNESS:

18 A Okay. So I was just saying that there's
19 an express disclosure in there about how the
20 Linnarsson range is 4 to 20, and we're talking
21 about combining the functions of the Linnarsson
22 cell tag barcode with the McCloskey random

1 amplification-bias-producing barcode.

2 So, at the very least, it contemplate --
3 it's expressly disclosed here that the -- you can
4 combine those two barcodes and use up to at least
5 20. So that range is explicitly written into this
6 paragraph.

7 BY MR. BAUGHMAN:

8 Q Okay. What is the number of nucleotides
9 that you provided for the barcode other than 7?

10 A Well, again, I think it -- the combination
11 of those can be up to 20, as were written there.
12 At the very least -- and that ignores all the
13 other disclosures talking about other possible
14 embodiments, but it's -- we're giving 7 as an
15 example, and that is not -- it's clearly written
16 as a nonexclusive example.

17 Q But the only example you provided even
18 though you say it's not exclusive?

19 A The only number I mention here
20 specifically is 7, but it's in the context of what
21 I believe would be clear to a POSA that it can be
22 optimized to fit the needs of their particular

1 experiment.

2 Q Could I ask you, please, to take a look at
3 your Exhibit 1059, your reply declaration.

4 A Okay.

5 Q And Paragraph 91, in particular.

6 A Okay.

7 Q Do you see there, Dr. Cooper you refer to
8 the McCloskey patent application US2007002640?

9 A In the footnote -- yeah, sorry. Yes, I
10 see that.

11 Q That's not an exhibit in this proceeding,
12 is it?

13 A I'm not sure one way or the other. I
14 don't think -- I don't know.

15 Q And, Dr. Cooper, you never referred to
16 that document in your original declaration,
17 Exhibit 1002, did you?

18 A Let me check for a second. I don't
19 believe so.

20 No, I can't find that number, so I don't
21 believe I referenced it, but I could be wrong, I
22 don't remember it, but I don't find it there.

1 Q Dr. Cooper, it's your opinion that
2 Linnarsson's CDS includes a sequence of thymines
3 that directs synthesis of a cDNA strand by
4 hybridizing with the poly-A tail of an mRNA stand,
5 right?

6 A It certainly does in some embodiments.

7 Q Sorry. I lost the audio for a second.
8 You probably answered, but I missed it. I'm
9 sorry.

10 A I said it does in some embodiments.

11 Q And those are embodiments that you used to
12 map to the claim language of the '981 patent,
13 right?

14 A Those are among the embodiments that I
15 used to map the claim language, yes.

16 Q Could I ask you, please, to turn to
17 Exhibit 1002 again. It's your original
18 declaration. And turn to Page 66.

19 A The Bates number or the page number?

20 Q I'm sorry, that's the actual native page
21 number. Good question.

22 And I accidentally closed my copy, so give

1 me a second.

2 I'm caught up. Are you on Page 66, which
3 is, using the numbers in the lower right,
4 1002.071?

5 A Yes.

6 Q And do you see there's a section heading
7 "[1C] generating a plurality of tagged
8 polynucleotides from the plurality of sample
9 polynucleotides"?

10 A Yes.

11 Q So is this part of your original
12 declaration where you are mapping your argued
13 coverage of that limitation of the claim?

14 A So I wouldn't -- I don't know if that's
15 the only place, but, yes, certainly this is where
16 I'm providing specific evidence relevant to that
17 claim limitation.

18 Q And specifically you're mapping limitation
19 1C here?

20 A Yes. Again, I can't be certain that that
21 nomenclature is the same. Was -- I think there
22 was some alphabetical number, but, 1C as defined

1 in the declaration, yes. I can't remember if that
2 was the same lettering that was used in the
3 original claim language but...

4 Q Understood.

5 And the claim language, however it was
6 numbered originally that we're talking about, is,
7 "generating a plurality of tagged polynucleotides
8 from the plurality of sample polynucleotides,"
9 right?

10 A That's right.

11 Q Okay. I'd ask you to turn a few
12 paragraphs forward to Paragraph 139.

13 Do you see that?

14 A Yes.

15 Q And that's still part of the same
16 discussion of limitation 1C?

17 A Yes.

18 Q And you say in Paragraph 139 that,
19 "Linnarsson first teaches using a tagged CDS
20 during cDNA synthesis to generate the tagged
21 cDNA," right?

22 A Yes.

1 Q And this is part of your mapping it to the
2 generating claim limitation 1C?

3 A Yes.

4 Q You go on to say, "For example, Figures 2
5 and 11 shown below depict an mRNA strand (boxed in
6 red, below) with a poly-A tail (highlighted in
7 red, below) and a CDS or tailed oligo-DT primer
8 (boxed in green, below) that directs synthesis of
9 a cDNA strand," right?

10 A Yes.

11 Q And you're pointing to both Figure 2 and
12 Figure 11 for that in the -- in the space beneath
13 the words, you've actually given an excerpt of
14 both of those figures from Linnarsson, right?

15 A That's correct.

16 Q And in both Figures 2 and Figure 11,
17 you're relying on the poly-A tail functionality as
18 part of generating tagged cDNA, correct?

19 A Well, in the context of Figures 2 and 11,
20 that's how the CDS is defined within those
21 particular embodiments, yes.

22 The CDS is the important part of that

1 process, and in this case, it's based on the
2 poly-A -- the poly-A sequence.

3 Q And in Paragraph 140, you say, "As
4 demonstrated in Figures 2 and 11 above, the CDS or
5 tailed oligo-DT primer includes a sequence of
6 thymines (highlighted in green, above) that
7 hybridize the sequence of adenines making up the
8 poly-A tail of the mRNA molecule," right?

9 A Yes.

10 Q And you say next, "This process is further
11 described in Linnarsson's figure description: 'A
12 reverse transcription step. A tailed oligo-DT
13 primer directs synthesis of the cDNA strand,'" and
14 it goes on, right?

15 A Yes.

16 Q And then in Paragraph 141, you continue
17 your discussion, and you say, "For example,
18 Figure 4 depicts an example of a CDS (boxed in
19 green, below) with a cell tag (highlighted in
20 green, below)," right?

21 A Yes.

22 Q And this is your mapping of limitation 1C

1 of the patent claim?

2 A Yes.

3 Q Dr. Cooper, you agree that bacteria are
4 prokaryotic, right?

5 A Yes.

6 Q They don't have a nucleus.

7 A Okay.

8 Q Do you agree with that?

9 A I think -- I recall 101 Biology, I think
10 most bacteria don't have nuclei. I can't -- I
11 wouldn't -- I'm not a bacteriologist. There could
12 be some that do; I really don't know.

13 Q But you would agree they're prokaryotic?

14 A Yes, they're often defined as prokaryotes,
15 yes.

16 Q Do you agree that only eukaryotic
17 organisms ordinarily have mRNA with a poly-A tail?

18 A I don't think that's true. I think there
19 are evidence of polyadenylation in some
20 prokaryotic organisms. I don't think it's used in
21 quite the same way or has the same mes- -- same
22 functionality. But I actually think there are

1 examples of poly-A-tailed mRNAs in bacteria.

2 Q Well, let me ask it this way: Do you
3 agree that only eukaryotic organisms have actively
4 transcribed mRNA with a poly-A tail?

5 A No, again, I don't agree with that. I
6 think there are bacteria that have poly-A tailed
7 RNAs.

8 Q Would you agree that mRNA polyadenylation
9 is absent in prokaryotic mRNAs except in
10 transcripts bound for degradation?

11 A No, I'm not comfortable saying that one
12 way or the other. Again, my understanding is that
13 some bacteria have poly-A-tailed mRNAs at their
14 ends.

15 Q Is it only when they're marked for
16 degradation?

17 A I don't --

18 Q You just don't know one way or the other?

19 A I don't know one way or the other. I
20 don't -- I don't necessarily think that's true,
21 but it's -- I -- but I'm not confident in that.

22 MR. BAUGHMAN: Okay. Let's go off the

1 record and take a break. It's been about an hour.

2 THE WITNESS: Okay.

3 (WHEREUPON, a recess was had.)

4 BY MR. BAUGHMAN:

5 Q Hi, Dr. Cooper. Are you familiar with the
6 journal "Cell"?

7 A Yes.

8 Q Is it a reputable journal?

9 A It's generally considered a strong
10 journal, yes.

11 Q During the break we added two exhibits to
12 the download area, and I've emailed them -- my
13 colleague emailed them to counsel for petitioner.

14 Could I ask you to try to open
15 Exhibit 2103 if you can.

16 (WHEREUPON, Exhibit No. 2103 was first
17 referenced.)

18 BY THE WITNESS:

19 A This is the Lloréns-Rico.

20 Q Yes.

21 A Yes, I have it.

22 Q And I'll just ask -- I assume the answer

1 might be no -- but have you read this article
2 before?

3 A I don't --

4 MR. WALTER: Hold on. Hold on. I'm going
5 to object for the record to the introduction of
6 this new exhibit. This is -- if I'm guessing
7 where this is going, this is something that should
8 have been introduced earlier, so I object to the
9 introduction of this document.

10 BY THE WITNESS:

11 A I can't say for sure one way or the other
12 whether I read it. I may have, but it doesn't
13 ring a bell at the moment.

14 BY MR. BAUGHMAN:

15 Q And I believe you testified a moment ago,
16 Dr. Cooper, that you weren't sure whether this
17 statement is correct, that: mRNA polyadenylation
18 is absent in prokaryotic mRNAs except in
19 transcripts bound for degradation.

20 Am I right that you weren't sure about
21 that?

22 A Yes, I -- yeah, that is fair.

1 Q I'd ask you to turn to the page in this
2 article with the number in the lower left corner
3 2728. And it's Table 1 in the article.

4 Do you see that?

5 A Okay.

6 Q And the fifth row down on the left, it
7 says, "Lack of polyadenylated mRNA"; do you see
8 that?

9 A Yes.

10 Q And in the text on the right in that row,
11 the first sentence is, "Many eukaryote-focusing
12 scRNA-seq approaches rely on poly(T) primers to
13 capture polyadenylated mRNAs. However, mRNA
14 polyadenylation is absent in prokaryotic mRNAs
15 except in transcripts bound for degradation."

16 Do you see that?

17 A I see that.

18 Q Does that change your view about whether
19 the statement is correct that mRNA polyadenylation
20 is absent in prokaryotic mRNAs except in
21 transcripts bound for degradation?

22 A No.

1 Q Do you have any reason to doubt whether
2 that statement in this article in "Cell" is true?

3 A I mean, I wouldn't necessarily say I doubt
4 it, but I generally treat everything with
5 skepticism, so I would want to do more digging on
6 that to address that question.

7 I think there's probably lots of
8 literature out there, and so I wouldn't be
9 comfortable, just because these authors wrote that
10 in this particular table, that that would be a
11 true statement. So, no, I would want to do more
12 digging on that point.

13 If I really wanted an answer that I was
14 comfortable with, I would have to do more digging.

15 Q And it's fair to say you didn't do that
16 digging before giving your opinion in Exhibit 1002
17 or in Exhibit 1059, right?

18 A I did not specifically address the
19 question of the fate of polyadenylated mRNAs in
20 bacteria, no.

21 Q So you didn't consider whether bacteria
22 have a poly-A tail?

1 A No. I believe there are some mRNAs in
2 bacteria that have a poly-A tail.

3 Q What are they?

4 A Again, that's -- that's where I don't
5 know. I believe they exist in bacteria, and I'm
6 just not sure of what's known about the
7 mechanistic usage of polyadenylation of bacteria,
8 the entire range of how mRNA processing happens in
9 bacteria. So I didn't do a deep dive on all the
10 possible fates of poly-A RNAs in bacteria, but I
11 believe there's evidence that they exist.

12 Q What is that evidence?

13 A I think we may have cited one, but I
14 can't -- I don't know.

15 Q Did you look for that evidence before you
16 rendered your opinions?

17 A I can't recall. I think it's something
18 that I had known in general or believed from past
19 experience, but I don't remember specifically what
20 I did for -- specifically for this document.

21 Q And you didn't discuss it in either of
22 your declarations, did you?

1 A Well, I believe we discussed in the
2 declarations about how the methods aren't
3 restricted to -- that the methods are applicable
4 to prokaryotic organisms.

5 Q But you said nothing about bacteria having
6 a poly-A tail in your declaration, either
7 Exhibit 1002 or Exhibit 1059?

8 A I'm not sure, but I maybe did not. I
9 don't know.

10 Q In your original declaration, did you ever
11 mention bacteria in connection with describing
12 Linnarsson at all?

13 A I may have. I don't recall doing so.

14 Q Why don't you take a look, Exhibit 1002.

15 A Again, I -- the -- if you look at, for
16 example, the Figure 1 description, it talked about
17 providing a sample, and so I -- I wouldn't --
18 certainly -- I don't think I addressed that
19 because I don't think I necessarily would have
20 read it to be restrictive. To exclude bacteria, I
21 guess is the point.

22 Q I'd like you to take a look at

1 Exhibit 2102, which should also be in your
2 download link now, and counsel should have a copy.

3 MR. WALTER: I'm going to object again to
4 the introduction of this exhibit as well.

5 (WHEREUPON, Exhibit No. 2102 was first
6 referenced.)

7 BY THE WITNESS:

8 A I have it.

9 BY MR. BAUGHMAN:

10 Q Are you familiar with the publication "BMC
11 Genomics"?

12 A Yes.

13 Q In your experience, is it a reputable
14 publication?

15 A Well, I guess I should -- it's a reputable
16 journal, so, yes, it includes a lot of
17 publications, but, yes, it's a reputable journal.

18 Q I'm going to call your attention to a
19 sentence in the abstract on the first page.

20 A Okay.

21 Q There's a heading that says "Background,"
22 and then there's a second sentence that says,

1 "However, unlike eukaryotic cells, mRNA sequencing
2 of bacterial samples is more challenging due to
3 the absence of a poly-A tail that typically
4 enables efficient capturing and enrichment of mRNA
5 from the abundant rRNA molecules in a cell."

6 Do you see that?

7 A I do.

8 Q And calling your attention to the last
9 paragraph on the same first page, the second
10 sentence says, "First, unlike in eukaryotes,
11 bacterial mRNA does not contain a poly-A tail at
12 the 3 prime end that can be used to easily enrich
13 for these molecules during reverse transcription."

14 Do you see that?

15 A I see it.

16 Q Were you aware that the prior art
17 contained statements like that at the time you
18 rendered your opinions in Exhibit 1002 and 1059?

19 A Well, I'm aware that the -- that
20 polyadenylation is fundamentally different between
21 bacteria -- eukaryotic bacteria and prokaryotic
22 and eukaryotic organisms.

1 Again, I don't think this statement is
2 true that there are never polyadenylated RNAs in
3 bacteria, so to the extent that they're arguing --
4 now, but it is true to say that it is
5 fundamentally different that -- whereas, in
6 eukaryotes, a large percentage of mRNAs are
7 polyadenylated. In bacteria, that's not true,
8 it's typically -- there -- a large percentage are
9 not polyadenylated. But that's different from
10 saying that it doesn't exist at all.

11 So I would agree that I was aware in
12 general that there's a very -- there's a
13 qualitative difference in the nature of
14 polyadenylation between prokaryotes and
15 eukaryotes, but I wouldn't agree with extreme
16 statements that say that it doesn't exist in
17 bacteria at all.

18 Q And I think you said there's a relatively
19 small percentage of bacteria for which there may
20 be poly-A tail; is that correct? That was your
21 understanding?

22 A Well, I think I would rephrase it as a

1 small percentage of the transcripts within any
2 given bacteria, but there could also be species
3 that break from that rule, right? I -- that, I'm
4 not sure one way or the other.

5 I think in general -- you might say, in
6 general, the rule for eukaryotes is that
7 transcripts are polyadenylated; in general, the
8 rule for bacteria is that they're not.

9 But that there's a huge amount of
10 variability within those statements that it's not
11 safe to say that -- just like it's not fair to say
12 that all eukaryotic transcripts are
13 polyadenylated, it's also not fair to say that all
14 bacterial transcripts are not polyadenylated is
15 what I would say.

16 Q Would you agree that you didn't do any
17 investigation to assure yourself of the frequency
18 with which bacteria have a poly-A tail or not
19 before you rendered your opinions in Exhibit 1002
20 and Exhibit 1059?

21 A I don't believe I did work beyond what I
22 felt comfortable saying in the declaration, no.

1 Q And you didn't in Exhibit 1002 say
2 anything about poly-A tails with bacteria, right?

3 A I don't believe so, no.

4 Q So do the statements in Exhibit 2102
5 change your view one way or the other?

6 A No.

7 Q Out of curiosity, do you know any of these
8 authors, Dr. Cooper?

9 A Do I know them personally?

10 Q Do you know of them?

11 A None of the names ring a bell. I may
12 have -- no, I don't think so.

13 Q Dr. Cooper, in your original declaration,
14 Exhibit 1002, do you say that your mapping of
15 Linnarsson's disclosures in this IPR don't use
16 biotin?

17 A So --

18 MR. WALTER: Hold on. Object to form.

19 BY THE WITNESS:

20 A I don't believe the word "biotin" appears
21 in my original declaration, so it's hard to answer
22 that question.

1 There are -- I would say throughout the
2 declaration, I often provide multiple sorts of
3 evidence within Linnarsson, so to the extent
4 you're talking about embodiments within Figure 11,
5 for example, those are usually accompanied by
6 looking at Figure 2, Figures 3, Figure 4 that have
7 nothing to do with biotin. So it's -- biotin is
8 certainly compatible with some embodiments of
9 Linnarsson, but by no means required.

10 BY MR. BAUGHMAN:

11 Q Well, in fact, in your declaration, you
12 cited to and included figures from Linnarsson that
13 do include biotin, correct?

14 A Yes, there are figures that have a
15 representation of a biotin label attached to some
16 primers, yes.

17 Q And you used those in mapping Linnarsson's
18 disclosures to the claim language, correct?

19 A I used those amongst other -- other pieces
20 of evidence and illustrations and disclosures,
21 yes.

22 Q And you didn't say in doing so that you

1 were excluding the biotin somehow, right?

2 A I did not address that because it's not --
3 it wasn't -- I didn't view it as germane to how
4 the language maps to the '981.

5 So, again -- but it's clear throughout
6 that there are embodiments that you can use biotin
7 as part of within Linnarsson, and there are
8 embodiments that don't require biotin that it
9 wouldn't be relevant to.

10 Q And in that original declaration,
11 Exhibit 1002, you didn't talk about making
12 modifications to the use of biotin in Linnarsson,
13 right?

14 MR. WALTER: Objection. Form.

15 BY THE WITNESS:

16 A Again, I would say I did not -- beyond the
17 inclusion of the biotin label in those figures, I
18 didn't discuss the biotin molecule because I
19 didn't feel it was particularly important.

20 BY MR. BAUGHMAN:

21 Q Let's go to Exhibit 1002, Paragraph 139
22 again.

1 Are you there?

2 A Yes.

3 Q And you recall that this is in your
4 discussion in the original declaration of
5 limitation 1C, correct?

6 A Yes.

7 Q And on Page 68 on the original numbering,
8 which is Page 1002.073 in the lower right, in
9 Paragraph 139, you include Figures 2 and 11,
10 correct?

11 A Yes.

12 Q And Figure 2, there's a black bar that you
13 don't (inaudible)?

14 (Reporter clarification.)

15 BY MR. BAUGHMAN:

16 Q In Figure 2 there is a black bar that you
17 do not explain?

18 A Well, I -- no, it's talked about as a
19 tailed oligo-DT primer. So that would be the
20 tail.

21 Q Okay. And in Figure 11, you have a green
22 box that includes within it the letters "BIO"; is

1 that right?

2 A Yes.

3 Q And that's biotin?

4 A Yes.

5 Q So you did mention biotin in your
6 declaration by including that figure, right?

7 A Yes. As I said, it's included in -- as
8 the -- represented as an imagine in that figure,
9 yes.

10 Q And looking at Paragraph 143 a little
11 further down.

12 A Okay.

13 Q Where it bridges onto Page 70, which is
14 also Page 1002.075, you see that you have referred
15 to Figures 2 and 11 together?

16 A Yes. They -- yeah, they appear side by
17 side, yeah.

18 Q And, again, in this Figure 11 excerpt that
19 you have included in Paragraph 143, there's biotin
20 on the right, correct?

21 A Yes.

22 Q Turning to the next page of your

1 declaration, right above Paragraph 148, you'll see
2 a heading indicating that we're moving into
3 limitation 1D, right?

4 A I'm sorry, there was an echo there.

5 Yes.

6 Q And turning to Paragraph 153 on Page 74,
7 also Page 1002.079, as part of your discussion of
8 limitation 1D, you included Figures 2 and 11,
9 correct?

10 A Yes.

11 Q And in Figure 11, there's a biotin shown
12 on the right of that excerpt you included,
13 correct?

14 A Yes.

15 Q And the same is true in Paragraph 154
16 where you include Figures 2 and 11, correct?

17 A Yes.

18 Q And turning ahead to the next page above
19 Paragraph 156, you'll see we're discussing
20 limitation 1E, correct?

21 A Yes.

22 Q And now turning within that discussion of

1 limitation 1E to Paragraph 164, you'll see a
2 statement in your text that says, "As shown below
3 in Figure 11, the TSO is added to the cDNA during
4 synthesis," correct?

5 A Yes, in that -- in Paragraph 163, there's
6 Figure 3 cited as well in the same context?

7 Q Right. Let's talk about that.

8 In Paragraph 163, you say, "Linnarsson's
9 Figure 3, as shown below, depicts using a TSO
10 comprising a cell tag" and so forth, right?

11 A Yes.

12 Q And then you continue in the next
13 paragraph and say, "As shown in" -- "As shown
14 below in Figure 11, the TSO is added to the cDNA
15 during synthesis," right?

16 A That's right.

17 Q So you're talking about "a TSO" in 163 and
18 "the TSO" in 164, aren't you?

19 MR. WALTER: Objection. Form.

20 BY THE WITNESS:

21 A So I believe we're talking about the TSO
22 in the context of Figure 11.

1 BY MR. BAUGHMAN:

2 Q Well, we're talking about the TSO in the
3 context of limitation 1E, right?

4 A Yes, and I'm providing multiple examples
5 of TSOs as disclosed in Linnarsson that map that
6 claim language of the '981.

7 Q And you say the, "TSO is added to the cDNA
8 during synthesis," right, in 164?

9 A And the same is true for the mention in
10 163 of Figure 3, yes.

11 Q Right. And, in fact, in Paragraph 164,
12 you talk about Figure 11 and cite it and include
13 it, and you also point at the same time to
14 Figures 2 and 3, right?

15 You say, "See also" -- I'm sorry. Scratch
16 that. That's the parallel document.

17 A Okay.

18 Q I may come back.

19 In Paragraph 164, there is biotin shown on
20 the right of the figure you included, right?

21 A Yes. It's a panel from Figure 11, yes,
22 with biotin.

1 Q And the same is true in 166; the panel
2 you've included there includes biotin on the
3 right, correct?

4 A Right. And the paragraph immediately
5 before it talks about Figure 4 in the same
6 context.

7 Q Right. And in Paragraph 165, which is the
8 one that's immediately before it, it says,
9 "Linnarsson disclosed a CDS," right?

10 A Yes.

11 Q And then in Paragraph 166, it says, "As
12 shown in Figure 11, the cell tag in the CDS,"
13 right?

14 A It says that, yes. Again, in the context
15 of for mapping multiple elements of Linnarsson
16 to -- multiple types of disclosure in Linnarsson
17 to this claim language.

18 Q Does it say anywhere that you're mapping
19 multiple types of disclosures instead of just
20 mapping what Linnarsson discloses?

21 A Well --

22 MR. WALTER: Objection. Form.

1 BY THE WITNESS:

2 A It's clear that we're talking about how
3 the -- how the tagging disclosed in Linnarsson
4 maps to the elements that are required in the
5 claim language, and I'm providing multiple lines
6 of evidence.

7 And these are both -- things -- there are
8 two different things called the TSO, two different
9 things called a CDS, and certainly a POSA would
10 understand that these are different versions of --
11 the function is to be a TSO or a CDS, and these
12 are different versions of that.

13 BY MR. BAUGHMAN:

14 Q Do you explain somewhere how to combine
15 the different embodiments that you're mapping as
16 you're saying it?

17 A I'm not understanding. There's -- I
18 map -- all the elements in '981 are mapped to
19 corresponding elements of Linnarsson and how they
20 are packaged together and the overall logic of the
21 process as outlined, and et cetera.

22 Q Well, as you hear you, it sounds like

1 you're saying there's a difference between what
2 you see in Linnarsson Figure 3 and what you see in
3 Linnarsson Figure 11.

4 I don't see a description of that in this
5 section under heading 1E, do you?

6 MR. WALTER: Objection. Form.

7 BY THE WITNESS:

8 A So, again, these are -- we're talking
9 about how Linnarsson uses TSOs and CDSs, and these
10 are different examples of structures of CDS and
11 TSOs and how they fit within the overall workflow.

12 So I feel like it's very clear that we're
13 talking about here's an example, here's another
14 example, here's another example, et cetera. All
15 of these map to that claim language.

16 BY MR. BAUGHMAN:

17 Q And limitation 1E is simply one of the
18 elements of the claim you're arguing about here,
19 right?

20 A Right, this is one step of claim 1.

21 Q And there are other steps -- like we just
22 looked at 1C and 1D, right?

1 A That's correct.

2 Q And I hear you saying now that you look at
3 these as different examples of CDSs and TSOs; is
4 that right?

5 A Well, if you -- I mean, the figure --
6 that's -- Linnarsson's calling saying here is a
7 CDS, here is an example of CDS, here is an example
8 of TSO, et cetera.

9 So the language in the Linnarsson
10 disclosure is very clear that these are
11 representative examples of how one might do this,
12 not --

13 Q And you --

14 A -- excluding.

15 Q Sorry.

16 And your declaration doesn't describe how
17 those examples are different, does it?

18 A Well, I'm -- in this case, I'm mapping
19 them to the specific claim language and how
20 they -- how each of them fulfills certain aspects
21 of the claim language.

22 So I'm focused on some degree of what they

1 have in common, which is, for example, an RNA
2 priming site, an amplification priming sequence,
3 the 4Gs at the end of the TSO, et cetera.
4 Those -- we're talking about the features that
5 TSOs have in common and CDSs have in common,
6 et cetera.

7 Q If you're saying that these are somehow
8 different, where in your declaration do you
9 explain which set of different disclosures you're
10 using across the different limitations 1C, 1D, 1E?

11 A So the point -- when we're talking about
12 the substance of each of the claim limitations and
13 mapping, those figure elements are bits of
14 evidence that map to the substance of the claim
15 language, so that's how that's being compared
16 there.

17 It's talking about what an MID is, what
18 the priming sites do, et cetera, so I'm mapping
19 each of those elements to the claim -- to the
20 required language of the claim.

21 Q But if you're now arguing that those bits,
22 as you called them, that you found in Linnarsson

1 are different from each other, where do you
2 explain how a person of skill would figure out how
3 to combine the different bits that you map across
4 1C, 1D, and 1E?

5 MR. WALTER: Objection. Form.

6 BY THE WITNESS:

7 A So I don't think they're -- they're not
8 different in how they fulfill the claim language
9 elements I guess is my point.

10 So we're talking about -- there's nothing,
11 for example, in the claim that requires a biotin,
12 so that's not really relevant to this portion.
13 They're talking about it has to have a tag. There
14 are other claims that say it has to have an
15 amplification priming site, et cetera.

16 So I'm talking about how the substance of
17 this -- of these figures in Linnarsson map the
18 substance of what's in the '981. And the
19 difference is, to the extent that there are
20 different embodiments of that that have other
21 optional features, that's not really relevant to
22 how they relate to claim 1 to the specific

1 limitations at issue.

2 BY MR. BAUGHMAN:

3 Q Figures 3 and 4 are both presented in the
4 context of Linnarsson's Example 1, correct?

5 A I'm not -- I mean, Figure 1 is a general
6 overview of a process that the CDSs and TSOs
7 described that are as representative Figures 3
8 and 4 can be used in that overall process.

9 Q I think you might have misheard my
10 question. I asked whether Figures 3 and 4 are
11 both presented in the context of Linnarsson's
12 Example 1?

13 A Oh, you said Example 1. I thought you
14 said Figure 1.

15 I'd have to review that to be sure. I
16 don't remember exactly how and when Linnarsson
17 uses that -- those figures.

18 Q You agree that that would be important,
19 though?

20 MR. WALTER: Objection. Form.

21 BY THE WITNESS:

22 A So I would agree that the CDSs and TSOs

1 serve important functions in Linnarsson, and to
2 the extent that the figures are giving a POSA
3 knowledge about how CDSs and TSOs -- like, what
4 their core functions are, what the design
5 constraints are, et cetera, I believe that's
6 important to the overall process.

7 BY MR. BAUGHMAN:

8 Q You agree that the place that an article
9 discusses a figure within its text might inform
10 the figure, right?

11 MR. WALTER: Objection. Form. Vague.

12 BY THE WITNESS:

13 A So, I mean, figures serve lots of
14 purposes. They can illustrate one specific point,
15 but they also provide general instruction. So I
16 think it's fair to say that Figures 3 and 4 are
17 important parts of the overall Linnarsson
18 disclosure.

19 BY MR. BAUGHMAN:

20 Q Would you agree that Figures 3 and 4 are
21 introduced and discussed only in Example 1 of
22 Linnarsson?

1 A I don't remember exactly how and when
2 Figures 3 and 4 are used, but to the extent that
3 Linnarsson refers throughout repeatedly --
4 right? -- to CDSs and TSOs, a POSA would
5 understand that Figures 3 and 4 are relevant to
6 any discussion of CDSs and TSOs because that's
7 giving you at least one flavor of how those could
8 be built.

9 Q So the same would be true of Figure 11;
10 that would apply to all discussions, right?

11 A In general, yes, so Figure 11 -- right? --
12 it talks about these are features that are
13 optional in the method. So I think a POSA could
14 rely on essentially -- I would agree that a POSA
15 is entitled to look at the whole document and
16 consider all of it -- all of the text and figures
17 and try to understand and interpret how the
18 methods are meant to work and what the practice of
19 steps is.

20 Q Let's open up Exhibit 1003, which is
21 Linnarsson, please.

22

1 (WHEREUPON, Exhibit No. 1003 was first
2 referenced.)

3 BY MR. BAUGHMAN:

4 Q You have it?

5 A One second.

6 Yes.

7 Q Okay. If you could turn to Page 1003.024.
8 Let me know when you're there.

9 A Okay.

10 Q Do you see at the top of the page there is
11 column 23?

12 A Yes.

13 Q And do you see the heading Example 1?

14 A Yes.

15 Q Do you recall how many examples there are
16 in Linnarsson?

17 A I don't.

18 Q I'll ask you to turn to Page 1003.032.

19 A Okay.

20 Q And that's column 31. Do you see that at
21 the top?

22 A I do.

1 Q And this is Example 2, correct?

2 A Yes.

3 Q Do you know of any other examples in
4 Linnarsson?

5 A I don't think so. What I'm saying is I
6 wouldn't necessarily exclude it, but those are the
7 two that -- yeah, I don't remember other ones.

8 Q Turning back to Example 1. If you go to
9 page to 1003.025.

10 A Okay.

11 Q The page after column 23. This is
12 column 24 now; do you see that?

13 A I do.

14 Q Do you see at the bottom paragraph, it
15 says, "The structure of a typical TSO shown in
16 Figure 3"?

17 A Yes.

18 Q So would you agree that that mention of
19 Figure 3 is inside of Example 1 in Linnarsson?

20 A I mean, it's certainly -- if you're -- in
21 terms of an organizational question, that's the
22 overall section it's in, but it's pretty -- the

1 language is pretty plain that this is the
2 structure of a typical TSO.

3 So, again --

4 Q And turning --

5 A -- would instruct a POSA that any time the
6 other mentions of a TSO occur, that this would be
7 informative for understanding how that's meant to
8 work.

9 Q And turning to the next column -- sorry --
10 the next page, which is 1003.026, which has
11 column 25 at the top.

12 Do you see that?

13 A Yes.

14 Q And do you see in the second
15 Paragraph there, the first full paragraph it
16 refers to Figure 4?

17 A I do.

18 Q So you'd agree that Figure 4 also as a
19 matter of organization appears inside Example 1 in
20 Linnarsson, right?

21 A Yes. And, again, uses the language that
22 it's the structure of a typical CDS, and it talks

1 about being able to insert additional arbitrary
2 sequences at various locations within the -- that
3 CDS. So it's clearly an open-ended description of
4 what a CDS can look like and how it might be used.

5 Q So you'd agree that Figure 4 and Figure 3
6 would be understood to be pertinent to Example 1
7 of Linnarsson, right?

8 A I would agree they are pertinent to the
9 understanding of Example 1 as well as a whole
10 range of other embodiments that are in scope of
11 Linnarsson.

12 Q And you'd agree that Example 1 of
13 Linnarsson discloses what you called fragmentation
14 and capture, right?

15 A It -- yes, it looks like biotin is at
16 least one component of the process, so that would
17 imply that they're doing a solid-phase capture,
18 yes.

19 Q And there's a heading on that same --
20 sorry -- on Page 1003.027, the next page that
21 says, "Bead capture and end repair/nick
22 translation," right?

1 A Sorry, which page are we looking at now?

2 Q I'm sorry. It's column 26, which is
3 numbered in the lower right 1003.027.

4 A Yes.

5 Q You see the heading near the bottom that
6 says, "Bead capture and end repair/nick
7 translation"?

8 A Yes.

9 Q And you agree that that's also part of
10 Example 1, right?

11 A Yes, I would.

12 MR. BAUGHMAN: This is probably a good
13 time for a break; it's 20 minutes before noon.
14 Let's go off the record.

15 (WHEREUPON, a recess was had.)

16 BY MR. BAUGHMAN:

17 Q Dr. Cooper, you refer in your declaration
18 Exhibit 1059 to next generation sequencing?

19 A Yes, I believe that appears, yes.

20 Q And is an abbreviation for that "NGS"?

21 A Yes.

22 Q Great.

1 It's your testimony that next generation
2 sequencing technologies at the time of the '981
3 patent could only accommodate short fragments; is
4 that right?

5 A Well, I think in general I said that, that
6 they were, for the most part, dominated by
7 short-read platforms which tend to produce reads
8 that are on the order of dozens to low hundreds,
9 yes.

10 Q In looking at Paragraph 7 of your reply
11 declaration, Exhibit 1059, I think that might be
12 the testimony you have in mind.

13 A Yes, that's right.

14 Q And you say in Paragraph 7 that, "These
15 NGS sequencing platforms are a short-read
16 sequencing platforms, meaning that the platforms
17 could only read relatively short stretches of DNA,
18 typically ranging from a few dozen to a few
19 hundred, correct?

20 A That's right.

21 Q And in Paragraph 8, you gave an example of
22 the Roche 454 NGS platform with an average read

1 length of about 250 base pairs per sample?

2 A I see that.

3 Q And you also give in Paragraph 8 an
4 example of Illumina NGS sequencing platform that
5 would only -- sorry -- that would read only dozens
6 to low hundreds of bases, right?

7 A That's right. And there are some exhibits
8 cited there, yes.

9 Q And jumping ahead to your Paragraph 63.
10 You similarly say -- are you there yet? I'm
11 sorry.

12 A Yeah, I'm there now.

13 Q Great.

14 In the third line, at the end, starting
15 there, "The next generation sequencing technology
16 at the time was limited to short reads to obtain
17 short fragments that the sequencing technology
18 could accommodate," right?

19 A I see that, yes.

20 Q And -- sorry this is out of order -- back
21 to 26. You say, "These platforms" -- I'll let you
22 get there first. Sorry. Paragraph 26.

1 A Okay.

2 Q Top of Page 15, which is 1059.018, you see
3 it says, "These platforms provide only short
4 stretches of sequence information from a
5 particular DNA fragment," correct?

6 A Yes.

7 Q Okay. So effectively NGS can only read
8 fragments as inputs; is that right?

9 MR. WALTER: Objection. Form.

10 BY THE WITNESS:

11 A So, I mean, I -- in this case I'm talking
12 about any particular DNA fragment. Fragment's
13 used in a very generic sense; it's just a DNA
14 molecule.

15 BY MR. BAUGHMAN:

16 Q And if a cDNA library in Linnarsson
17 contained full-length cDNA samples rather than
18 fragments, you'd need to fragment the cDNA to
19 sequence it using NGS, right?

20 A I don't think that's necessarily true. It
21 would greatly depend on how you did the cDNA
22 library prep and what sort of sample preparation

1 procedures went into that.

2 If, for example, you were looking at cDNAs
3 that were lower -- that were shorter than the
4 length of your sequencing run -- which certainly
5 there are examples of short cDNAs -- that would be
6 accommodated in, say, a few hundred base pairs.
7 So that would really depend on the particulars of
8 the experiment.

9 Q And if the cDNA fragments in the library
10 were too long, you might need to do further
11 fragmenting to sequence using NGS, right?

12 A Again, it depends on the goals of the
13 experiment. You would -- you would potentially
14 want to fragment, or you might be comfortable
15 getting only portions of the molecule read out
16 or -- you know, it would all depend on the
17 particular details of what the experiment was and
18 what the artisan was hoping to get out of it.

19 Q But it could be true?

20 A It certainly could be true that you would
21 fragment to get it to a size that you want to
22 optimize for your -- for your sequencing reaction.

1 Q After creating a library?

2 A I think there would be a number of
3 protocol where -- I don't know about the timing
4 there, but at some point before you put it on the
5 sequencer.

6 Q And you've testified about library
7 preparation itself being accomplished by
8 fragmenting, correct?

9 A I don't think I said -- certainly didn't
10 say that as a matter of exclusion that you have to
11 do fragmentation as part of library prep. I think
12 it can be part of a library prep or procedure, but
13 I wouldn't say it's always a requirement.

14 Q Looking at your original declaration,
15 Exhibit 1002, at Paragraph 97, please. Let me
16 know when you're there.

17 A Okay.

18 Q You see it begins, "Library preparation is
19 often accomplished by random fragmentation of
20 input DNA"?

21 A Yes.

22 Q You agree that that's correct?

1 A Yes. Is often accomplished, yes.

2 Q And you would agree that Linnarsson
3 discloses that further fragmenting could be done
4 after Figure 11, right?

5 A I don't remember if I said that or not,
6 but I -- certainly one would contemplate many
7 fragmentation steps if one wanted to.

8 Q And do you recall whether the Linnarsson
9 discussion includes shotgun sequencing?

10 A I don't recall. If we could pull up the
11 patent, we can look, but I don't remember one way
12 or the other.

13 Q Sure. If we could pull up Exhibit 1003,
14 if you could take a look, please, at column 22.

15 A Okay.

16 Q I'm sorry, this is Page 1003.023. You'll
17 see around Line 14 it defines shotgun sequencing,
18 correct?

19 A Yes, I do see that.

20 Q Turning back to your reply declaration,
21 your new declaration, Exhibit 1059, please, at
22 Paragraph 65.

1 A Okay.

2 Q You say that, "As described in my prior
3 declaration, Linnarsson broadly discloses a
4 sequencing step that does not refer to any sort of
5 fragmentation and does not include the steps of
6 Figure 11," correct?

7 A That's right.

8 Q And you cite to your original declaration,
9 Paragraphs 195 to 199, right?

10 A Yes.

11 Q Let's look at Paragraph 198 in your
12 original declaration. That's Exhibit 1002.

13 A Okay.

14 Q And do you see, Dr. Cooper, that that's
15 within the discussion of limitation 1G of the
16 claims?

17 A Yes.

18 Q So you're discussing here how you argue
19 your prior art combination discloses sequencing
20 the plurality of tagged polynucleotides to obtain
21 a plurality of identified polynucleotide
22 sequences, right?

1 A Yes.

2 Q And turning back to Paragraph 198 on
3 Page 1002.099.

4 You're citing, in part, column 21 of
5 Linnarsson at lines 13 to 25, correct?

6 A Column -- it looks like it's column 19, 28
7 to 32? Or am I not looking at the right place?

8 Q Sorry. Yeah, I should have given you a
9 hint. If you look at the next page where that
10 block quote at the bottom ends, do you see that
11 citation --

12 A Okay.

13 Q -- the long block quote from Pages 94 to
14 95 for --

15 A Right, there are two -- there are two
16 block quotes there --

17 Q Yeah, it's the second block quote. So let
18 me ask a cleaner question.

19 In your Paragraph 198, Dr. Cooper, you
20 agree that the second block quote there is from
21 Linnarsson Exhibit 1003 at column 21, lines 13 to
22 25?

1 A Yes. The second block quote, yes.

2 Q And that, again, is included in your
3 citations for covering limitation 1G of the patent
4 claims?

5 A Yes.

6 Q Okay. And you're talking here about a
7 sequencing step; that's what your introduction at
8 the beginning of Paragraph 198 says?

9 A Yes.

10 Q Okay. Looking just at the first couple
11 words of this block quote, it says, "The method of
12 preparing a cDNA library described herein,"
13 correct?

14 A Correct.

15 Q And you'll recall that Linnarsson defines
16 a cDNA library, right?

17 A I'm sure it does. And I can't remember
18 exactly what definition it uses, but yes.

19 Q Sure. I'll take you there. So let's look
20 at Exhibit 1003, which is Linnarsson, at
21 column 12, lines 4 to 8.

22 A Yes.

1 Q And you see it refers to -- sorry -- it
2 says this: "The term 'cDNA library' refers to a
3 collection of cloned complementary DNA (cDNA)
4 fragments which together constitute some portion
5 of the transcriptome of a single cell or a
6 plurality of single cells," correct?

7 A Yeah. It goes on to provide additional
8 information, but, yes, that's the start of --

9 Q Sure. It goes on to say, "cDNA is
10 produced from fully transcribed mRNA found in a
11 cell, and, therefore, contains only the expressed
12 genes of the single cell or, when pooled together,
13 the expressed genes from a plurality of single
14 cells," correct?

15 A Yes.

16 Q So you agree that in the words of
17 Linnarsson, the cDNA library refers to a
18 collection of cloned complementary DNA fragments?

19 A Yes, but I would not agree with the
20 implication that it requires fragmentation; it's
21 referring to fragments as a term for molecules.
22 And, in fact, it talks about fully transcribed

1 mRNA, for example. So I think they would consider
2 a full-length mRNA to also be a, quote, fragment,
3 but it doesn't imply fragmentation as an active
4 step.

5 Q Is it your testimony that cDNA is always
6 fragmented?

7 A I think in the context of this paragraph,
8 the way Linnarsson is using it, they're using
9 fragment in a general way, which would include
10 full-length mRNAs and full-length cDNAs.

11 It's a fragment in the sense of it's not
12 one long contiguous -- it's not like a whole
13 chromosome; it's a portion of a DNA mole- -- or an
14 RNA molecule, it's not a -- again, it doesn't
15 imply an active fragmentation step as a verb; it's
16 just using it as a noun in a generic way.

17 Q So is that because your -- in your view,
18 cDNA is always understood to be a fragment?

19 A I think it's the way Linnarsson is using
20 that terminology. In this case I wouldn't say
21 that that applies everywhere in all possible
22 publications; it's just this is how Linnarsson is

1 coining that.

2 Q But that is your view of how Linnarsson
3 understands cDNA?

4 A I believe that they would encompass --
5 fragments could mean full-length, and it could
6 also means portions thereof. I think it's a
7 general definition which encompasses both.

8 Q So essentially the word "fragments" in
9 line 5 of column 12 is meaningless; it doesn't add
10 anything to the sentence; is that what you're
11 saying?

12 MR. WALTER: Objection. Form.

13 BY THE WITNESS:

14 A No, I don't think so. I think it's
15 telling you that it's a cDNA molecule. It has --
16 it's an actual cDNA. It's a -- so I just don't
17 think it limits the nature of what those molecules
18 are in terms of how they're produced.

19 BY MR. BAUGHMAN:

20 Q So --

21 A Certainly not meaningless.

22 Q What does it add to the word "DNA" or

1 "cDNA" if they're already assumed to be a
2 fragment?

3 A Well, it outlines the numerosity of the
4 fragments, for example. It's -- you're talking
5 about the library including multiple sets of cDNA
6 molecules. It's giving you -- so it's -- yeah.

7 Q The word "fragments" indicates the
8 numerosity of the molecules?

9 A Well, it's a plural noun, so it's
10 certainly -- it's -- the library's referring to
11 multiple fragments. As opposed to a single cDNA,
12 for example.

13 Q So its purpose is to say that there are at
14 least two -- two complementary DNA or cDNA?

15 A Well, again, I think it's sort of working
16 almost the same way as molecules. It's -- so you
17 need some word there I think is the point. You
18 need an add word, and I think there -- again,
19 especially given the later context that they're
20 talking about fully transcribed mRNA, it's clearly
21 an inclusive definition that talks about molecules
22 that are cDNA molecules in general.

1 Q But Linnarsson chose the word "fragments"
2 here?

3 A Yes. Plainly they did, yes.

4 Q So going back to your Paragraph 198 in
5 Exhibit 1002. Sorry to jump around.

6 Are you with me?

7 A Okay.

8 Q So we were looking at this block quote
9 from Linnarsson that you included in
10 Paragraph 198.

11 A Yes.

12 Q And where you see, "The method of
13 preparing a cDNA library described herein." And
14 whatever the meaning of fragments, we agree that
15 it's defined -- cDNA library in Linnarsson is
16 defined to be cDNA fragments, correct?

17 A With the additional context in that
18 paragraph, yes.

19 Q And then the sentence goes on to say, "Can
20 further comprise processing of the cDNA library to
21 obtain a library suitable for sequencing," right?

22 A Correct.

1 Q And that's -- further processing is
2 described in this block quote is more fragmenting,
3 quote, to obtain a short-fragment 5 prime end
4 library, end quote, that's suitable for next
5 generation sequencing, right?

6 MR. WALTER: Objection. Form.
7 Mischaracterizes the document.

8 BY THE WITNESS:

9 A So the -- it says "can be processed by
10 fragmenting," so I think that is indicative of
11 this is just one example of a step that one can
12 take to put it on a sequencer.

13 BY MR. BAUGHMAN:

14 Q Okay. And that's the further processing
15 that's referred to in the first sentence?

16 MR. WALTER: Objection. Form.

17 BY THE WITNESS:

18 A I think it talks about, yeah, further
19 comprising. So it's talking about steps that can
20 be taken as part of processing, which -- one of
21 which step is that it's possible to process by
22 fragmenting.

1 And I should say that this to me indicates
2 that the fragment in this -- of the -- in the use
3 of the cDNA library is more general because
4 they're talking about an additional fragmentation
5 step. Which you wouldn't do if you were already
6 done, right? If you had already done
7 fragmentation, you wouldn't necessarily do it
8 again. So --

9 Q Well, as we discussed -- as we discussed
10 earlier -- sorry. Are you finished, Dr. Cooper?

11 A Yes.

12 Q As we discussed earlier, you said that for
13 NGS, if the sequences are too long, you could have
14 a need to fragment them further, correct?

15 A Correct, you can. You wouldn't
16 necessarily always need to, but it's possible.

17 Q So turning back to Exhibit 1059, your
18 reply declaration, in Paragraph 65.

19 A Yes.

20 Q The range of citations is 195 to 199. We
21 just looked at Paragraph 198, correct?

22 A That's right.

1 Q And it does, in fact, refer to
2 fragmentation, correct?

3 A It mentions fragmentation as one possible
4 step that can be used as part of sequencing, yes.

5 Q And it did that in a portion that you
6 block quoted as part of your discussion of the
7 claim limitation, right?

8 A It did that in one portion of one block
9 quote in the context of multiple block quotes,
10 yes.

11 Q And those were block quotes you chose to
12 put in your declaration for limitation 1G?

13 A That's correct.

14 Q Now looking at Paragraph 70 of your reply
15 declaration, Exhibit 1059.

16 A Okay.

17 Q Actually, no. Let's skip that.

18 Okay. In Paragraph 27 of your
19 declaration, this is Exhibit 1059. I'm going to
20 ask you to go there.

21 A Okay. One moment.

22 Okay.

1 Q Are you there?

2 A Yes, the section, "The '981 patent"?

3 Q Yes.

4 And is it your view that Dr. Quackenbush
5 ignores Figures 3 and 4 of Linnarsson?

6 A I'm sorry, this is about -- this part of
7 my declaration is talking about the '981 patent.

8 Q I'm sorry, I'm on Paragraph 27 of your
9 declaration, Exhibit 1059.

10 A Oh, 1059. Sorry.

11 Q Yeah, your reply declaration.

12 A Okay. Hold on. So we're in Paragraph 27
13 of the 1059; is that right?

14 Q Yeah.

15 A Yes.

16 Q And it sounds like you're saying his
17 declaration ignores Figures 3 and 4, correct?

18 A That's right. To the extent that his
19 argument was heavily predicated upon concerns
20 about how biotin and -- how a biotin would limit
21 certain protocols, that that would ignore the
22 disclosures in Figures 3 and 4 that clearly

1 indicate that biotin is not required for CDS or
2 TSOs.

3 Q And you'll agree that Dr. Quackenbush
4 actually talked about Figures 3 and 4 in his
5 declaration, right?

6 A I don't remember exactly how he -- if or
7 how he discussed Figures 3 and 4. I'd have to
8 look at the declaration. I don't remember
9 exactly.

10 Q So it's not your testimony that he didn't?

11 A Well, it might -- in this page what I'm
12 talking about is the -- there was this
13 overwhelming focus from his declaration about the
14 limitation of Figure 11 and the restrictions on
15 how that would make it difficult for a POSA to use
16 the protocol. And my point that is just incorrect
17 because it ignores the fact that the Linnarsson
18 disclosure is generic and does not require
19 the specific -- all the details that are disclosed
20 in Figure 11.

21 Figure 3 and --

22 Q Okay. So you --

1 A -- 4 are prominent examples.

2 Q You weren't meaning to say that
3 Dr. Quackenbush didn't point to either of them?

4 A Again, I think he did not -- if he did
5 discuss them, he did not discuss them to the
6 degree that I felt they were warranting discussion
7 of the overall disclosure.

8 Q Let's look at your Paragraph 34, please,
9 in Exhibit 1059.

10 A Okay.

11 Q About three lines in you say -- or two
12 lines in, sorry, "Linnarsson discloses embodiments
13 that are distinct from the approach of Figure 11,"
14 correct?

15 A That's right.

16 Q And you say, "For example, in Figures 3
17 and 4, Linnarsson disclose a TSO and CDS that are
18 incompatible with a fragmentation and capturing
19 approach set forth in Figure 11," right?

20 A That's right.

21 Q We discussed already that Figures 3 and 4
22 are present within Linnarsson's Example 1, right?

1 A Yes, with the caveat that they are
2 informing any time -- so they talk about a typical
3 CDS or a typical TSO, so, in my opinion, they
4 inform other parts of the document as well.

5 Q And you've testified that Linnarsson's
6 Example 1 discloses fragmentation and capture,
7 correct?

8 A That's right.

9 Q Now, to say that Figures 3 and 4 are
10 incompatible with fragmentation and capture, you
11 argue that each of them lacks any restriction
12 enzyme cut site; is that correct?

13 A I think that's part of the argument, yes.

14 Q Okay. Looking at your Paragraph 66,
15 please. Let me know when you're there.

16 A Of the 1059 still?

17 Q Of 1059. Thanks for asking.

18 A Okay.

19 Q You will see that you say that
20 Linnarsson -- let me find it myself here on the
21 page. One second.

22 "Linnarsson's Figure 3 and Figure 4 show

1 exemplary TSO and CDS that" -- and I'm jumping
2 ahead a little here -- "do not contain any enzyme
3 restriction cut site."

4 Do you see that?

5 A So you're in Paragraph --

6 Q 66.

7 A Okay.

8 Q Starting five lines down or so on the
9 right.

10 A Yes.

11 Q "Linnarsson contains numerous exemplary
12 embodiments that do not include any restriction
13 enzyme cut site." You also argue biotin; is that
14 right?

15 A If -- yeah, about midway through
16 Paragraph 66, yes, Linnarsson contains -- yeah,
17 "numerous that do not include a biotin or a
18 restriction enzyme cut site."

19 Q And then a few lines down you say -- or,
20 sorry, one line down you say, "For example, as
21 discussed at length in my prior declaration and
22 above, Linnarsson's Figure 3 and Figure 4 show

1 exemplary TSO and CDS," right?

2 A Yes.

3 Q And then a little further in that
4 sentence, you say, "They do not contain any
5 restriction enzyme cut site," correct?

6 A That's right.

7 Q What work did you do in looking at
8 Figures 3 and 4 before you opined that they didn't
9 contain any restriction enzyme cut site?

10 A Well, I looked for the cut site that is
11 referred to in Figure 11, and it's absent from
12 that. The Figure 11 cut site is not present
13 inside Figures 3 and 4. I think they call it BTS
14 or BtsCI.

15 Q Did you look for any other cut site?

16 MR. WALTER: Objection. Form.

17 BY THE WITNESS:

18 A No, I did not.

19 BY MR. BAUGHMAN:

20 Q You'll agree that people of skill at the
21 time of the '981 patent had resources available to
22 identify restrictions on cut sites, right?

1 A Yes.

2 Q Have you ever heard of New England
3 Biolabs?

4 A Yes.

5 Q Are you aware that they put out
6 publications and posters that show enzyme cut
7 sites?

8 A That is one of their main products, yes.

9 Q Do you know of something called the
10 NEBcutter website?

11 A It rings a bell. I'm sure I've been there
12 before, but, yes, I don't remember what it's
13 called exactly.

14 Q And are you familiar with New England
15 Biolabs being abbreviated "NEB"?

16 A Yes.

17 Q Would it surprise you to learn you can
18 type in a sequence in the NEBcutter website and
19 find out what restriction enzyme cut sites there
20 are in it?

21 A Nope.

22 Q Did you do any investigation of the

1 sequences in Figures 3 or 4 to see if they had
2 enzyme cut sites?

3 A Again, my focus was on the -- this cut
4 sites that are referred to in Figure 11, and
5 that's what I was confident saying. So I did not
6 search for the universe of all possible
7 restriction enzyme cut sites.

8 Q So just the one, the restriction enzyme in
9 Figure 11, cut site?

10 A That's right, that's the one I focused on.
11 And the fact that the only sequence besides the
12 guanines that's used for the template switching
13 and the cell tag is the priming site for the
14 amplification for the PCR cell.

15 Q Let's take a look at --

16 A (Indiscernible.)

17 Q -- Exhibit -- I'm sorry?

18 A Yeah, so the -- you know, all of the
19 sequence elements in Figure 3 and 4, the purpose
20 of every base pair is accounted for within
21 Linnarsson. One's a priming site, a cell tag, and
22 a template switching step.

1 So to the extent that there are cut sites
2 that happen to be in there, I don't think
3 Linnarsson contemplated that you would necessarily
4 use them because those sequence elements are for a
5 different purpose.

6 Q Well, let's take a look at Exhibit 1003,
7 which is Linnarsson Figure 3, please.

8 A Okay.

9 Q Let me know when you're there.

10 A Okay.

11 Q So starting from the 5 prime end here of
12 Figure 3, if you look at the third base, you'll
13 see a G for guanine, right?

14 A Yes.

15 Q And the pattern there is GCAGTG, correct?

16 A Yes.

17 Q Do you know one way or the other whether
18 that's a restriction enzyme cut site?

19 A I don't.

20 Q What's the restriction enzyme in
21 Figure 11?

22 A I think it's what we talked about, BTS or

1 BtsCI I think they refer to it.

2 Q Would it surprise you to know that CG --
3 sorry -- GCAGTG is the restriction enzyme cut site
4 for BtsI?

5 A So there -- I was a little confused in
6 here. I think there are -- BTS is -- and I define
7 the cut site that Linnarsson refers to as GGATG,
8 not GCATG.

9 Q Right. I'm asking about a different
10 sequence. I'm asking whether it would surprise
11 you to know that GCAGTG is a restriction enzyme
12 cut site for BtsI?

13 A I'd have to do the details on that.
14 It's -- it could be a cut site for a different
15 enzyme than that which is disclosed in Linnarsson.
16 It may be.

17 Q So you don't know one way or the other?

18 A That's right.

19 Q And if we look at Figure 4, also three
20 bases in you'll see GCAGTG again, right?

21 A That's right.

22 Q So if that's a restriction enzyme cut site

1 for BtsI, it's in both Figures 3 and 4, correct?

2 A That stretch of nucleotide is there, yes.

3 And, again, we're referring to an enzyme that
4 Linnarsson doesn't elsewhere refer to.

5 Q And you don't have an understanding one
6 way or the other about whether that is such a cut
7 site?

8 A I don't, but I don't think it's -- again,
9 I don't think it's part of Linnarsson's disclosure
10 even if it is a cut site for a different enzyme
11 that happens to be in the NEB catalogue.

12 Q But you based your opinion in the reply
13 declaration on the fact that there isn't any
14 enzyme cut site in Figures 3 and 4, correct?
15 That's what you say.

16 A As one component of an overall opinion,
17 and, again, with the focus being on the cut sites
18 that Linnarsson actually did disclose as how
19 they're used in Figure 11.

20 Q Well, in Paragraph 66 you say, "any
21 restriction enzyme cut site," correct?

22 A I do.

1 Q And in Paragraph 42, you say, "lack of a
2 restriction enzyme cut site," you don't say the
3 one in Figure 11. Does that surprise you?

4 A Well, let me look at Figure -- you said
5 42?

6 Q 42, yeah.

7 A Well, I say that, "It cannot be the case
8 that Linnarsson is contemplating the fragmentation
9 and capture of Figure 11 and all its embodiments
10 because the restriction enzyme cut site that is
11 needed to release the fragments following capture
12 is also absent from Figure 3."

13 So this is clearly in the context of the
14 method disclosed by Figure 11 including the enzyme
15 that is part of that can't be part of what's used
16 in Figure 3.

17 Q Is it your testimony that Figure 11
18 wouldn't work with a different enzyme and cut
19 site?

20 A I wouldn't say one way or another. I'm
21 saying it's clearly very different from what's in
22 Figure 11, which is a specific enzyme and a

1 specific cut site. And so it's different, and
2 Linnarsson didn't describe if there was a
3 different enzyme or a different cut site that
4 would be used.

5 But there clearly --

6 Q You say --

7 A -- (indiscernible) --

8 Q Sorry. You say BtsI and BtsCI are very
9 different?

10 A I'm saying they're different enzymes that
11 have different recognition cut sites so they will
12 behave differently.

13 Q And in Paragraph 42, you start off by
14 saying, "The lack of a restriction enzyme cut site
15 in biotin in Figure 3 is critical," right?

16 A If you finish that sentence, it's related
17 to the fragment and capture approach of Figure 11.
18 So that carries with it the specific details of
19 the other aspects of Figure 11 including the
20 particular cut site that is used.

21 Q And you agree that -- you don't -- you
22 haven't formed an opinion one way or the other

1 about whether another cut site and enzyme would
2 work in Figure 11?

3 A Again, I don't -- I'm saying it's not the
4 same as Figure 11. And I'm saying it also lacks
5 things like a biotin on it, so it's very -- again,
6 qualitatively a very different method in my
7 opinion.

8 Q Is it your testimony Figure 11 only works
9 for the specific sequence listed in Figure 11?

10 MR. WALTER: Objection. Form. Vague.

11 BY THE WITNESS:

12 A I don't think that's true of all possible
13 embodiments. I'm saying that it's a very specific
14 example that, if you were to redesign it, could it
15 work other ways? Maybe. I don't know.

16 BY MR. BAUGHMAN:

17 Q Maybe with a different enzyme and cut
18 site?

19 A With potentially other changes, perhaps.
20 The one thing you can't do is, if there's no
21 biotin, you can't use beads -- right? -- you can't
22 use stripped without a biotin molecule, so it's --

1 again, we're sort of doing apples to oranges here.

2 Q Well, you testified in Paragraph 31 that a
3 restriction enzyme cut site is part and parcel of
4 the fragmentation method, right? It's something
5 you testified about as part of the basis of your
6 opinion?

7 A Yes.

8 Q Okay. And you don't know one way or the
9 other sitting here today whether Figures 3 and 4
10 actually do contain restriction enzyme cut site,
11 do you?

12 A I am confident Linnarsson did not describe
13 that or mention that in there, but it's possible
14 that it includes one as sort of happenstance, yes.

15 Q What basis do you have for saying it's
16 happenstance?

17 A Because they define the function of every
18 other base within that, and so I think if they
19 intended you to have a cut site, they would have
20 pointed out the fact that there's a cut site here
21 of -- every base has a part of a functional
22 designation within Figures 3 and 4, and no cut

1 site is mentioned; whereas, in Figure 11, they
2 actually do say here's the cut site.

3 So I would assume that Linnarsson, if they
4 intended a cut site to be used there, they would
5 have highlighted it.

6 Q For example, by describing a cut site in
7 Example 1 and then citing to Figures 3 and 4?

8 A Not necessarily. I think those --
9 Figures 3 and 4 are disclosing different aspects
10 in that context of Example 1. For example, the
11 4Gs, the templates. So there are lots of other
12 aspects of Figures 3 and 4 that are relevant to
13 Example 1, not necessarily all.

14 Q Is there any other part of the Example 1
15 that suggests to you that this would be done
16 without a cut site?

17 A I mean, I -- well, I -- to the extent that
18 Linnarsson provides a more general method, that --
19 I think there are other protocols that one could
20 use, but Example 1 itself clearly used biotin at
21 cut sites.

22 Q What more general method do you have in

1 mind? Figure 1?

2 A One that doesn't rely on any biotin
3 pulldown, right? So Figures 3 and 4 provide
4 primers that have no biotins, so clearly there's
5 no biotin required for the function of those CDSs
6 or TSOs to function. So embodiments that use
7 those without biotin has a --

8 Q Do you --

9 A -- figure would function that way.

10 Q Sorry. You agree that Example 1 talks
11 about biotin, right?

12 A Example 1 includes biotin, yes.

13 Q And Figures 3 and 4 are introduced inside
14 of Example 1, right?

15 A They are discussed there, yes. But,
16 again, I would read that as a POSA would read it,
17 which is that the figure is informative to not
18 just that one example, but to the structure of the
19 method as a whole.

20 Q So where is this embodiment in Linnarsson
21 that doesn't use a cut site or a biotin?

22 A So the claims, for example, the -- claim 1

1 of Linnarsson doesn't refer to fragmentation or
2 cutting.

3 Q Does that mean that Linnarsson doesn't --
4 provides an example of doing something without it?

5 A I think they're clearly disclosing an
6 overall process that doesn't require it.

7 Q Did you cite claim 1?

8 A I did.

9 Q Where?

10 A So, at the very least, when looking at --
11 focusing on whether the Linnarsson provisional is
12 supportive of the Linnarsson claims, there's a
13 detailed claim chart which walks through each of
14 the portions of claim 1 and talks about how the
15 disclosure provides support to each one of those
16 claim elements.

17 Q Did you map claim 1 of Linnarsson to any
18 disclosure -- sorry -- to any claim in the patent,
19 in the '981 patent?

20 A There -- well, so there -- to the extent
21 that that chart connects specific aspects of
22 Linnarsson's disclosure to claim language

1 elements, I -- there's lots of overlap in the
2 claim elements. I focused more on the disclosure
3 in the specification, but there's clearly a very
4 strong connection between the claim 1 elements in
5 Linnarsson with aspects of the specification in
6 Linnarsson that then relate to the '981 patent
7 claims.

8 Q But what you're testifying to is that you
9 did that analysis in the context of showing that
10 Linnarsson has support for its provisional, not in
11 mapping the claims, right?

12 A Except it also maps it to particular
13 elements of text within the specification of
14 Linnarsson, which are themselves mapped to claim
15 elements of the '981.

16 MR. BAUGHMAN: Let's go off the record for
17 a second.

18 (WHEREUPON, a recess was had.)

19 (WHEREUPON, Exhibit No. 2101 was first
20 referenced.)

21 BY MR. BAUGHMAN:

22 Q Dr. Cooper, I think you have before you

1 Exhibit 2101 now; is that correct?

2 A Yes.

3 MR. WALTER: And we'll object again to the
4 introduction of this exhibit.

5 BY MR. BAUGHMAN:

6 Q Dr. Cooper, do you recognize any of the
7 authors of this paper?

8 A No.

9 Q You see they're from New England Biolabs,
10 correct?

11 A Yes.

12 Q And that's an entity with which you are
13 familiar?

14 A Yes.

15 Q And they're prominent in the field of
16 enzyme restriction sites and so forth?

17 MR. WALTER: Objection. Form.

18 BY THE WITNESS:

19 A They're a company that sells a lot of
20 restriction enzymes, yes.

21 BY MR. BAUGHMAN:

22 Q You'll see that in the abstract, the first

1 line says, "The Type IIS restriction endonuclease
2 BtsI recognizes and digests at GCAGTG (2/0),"
3 correct?

4 A Yes, I see that.

5 Q And then in right column on the same page
6 at the top, it says, "The cleavage sequence is
7 GCAGTG (2/0), which means that BtsI cuts 2nt" --
8 or nucleotides -- "after the recognition sequence
9 on the top strand and right after the recognition
10 sequence on the bottom strand."

11 Do you see that?

12 A Sorry. I lost where you're reading that
13 in --

14 Q Sorry. Page 1 of Exhibit 2101.

15 A Yeah.

16 Q Right column.

17 A Oh, right column. Okay.

18 Q My fault if I said left. Right column,
19 second line starting with "The."

20 Do you see that?

21 A I do.

22 Q So it says, "The cleavage sequence is

1 GCAGTG (2/0), which means that BtsI cuts 2nt" --
2 or nucleotides -- "after the recognition sequence
3 on the top strand and right after the recognition
4 sequence on the bottom strand," correct?

5 A That's right.

6 Q Were you --

7 A I see that.

8 Q Sorry. You see that.

9 Were you aware that this statement had
10 been made in the art before you rendered your
11 opinion in Exhibit 1059?

12 A I don't recall reading this paper, no.

13 Q Does it refresh your recollection one way
14 or the other about whether GCAGTG is an enzyme
15 restriction site?

16 A Again, I'd have to read through this
17 paper. I don't -- it's from New England Biolabs,
18 and that's what they're saying, but I -- you know,
19 it's hard to -- these are New England Biolabs
20 authors in a PLOS One paper; I'd have to do more
21 homework on this. I don't...

22 Q And you didn't do that before you

1 testified that there were no restriction sites in
2 Figures 3 and 4, right?

3 A I did not look at this paper.

4 Q Or do other investigation, did you?

5 A I did not look for the universe of all
6 theoretical restriction enzyme cut sites.

7 Q Did you look for any cut sites before the
8 ones specifically given as an example in
9 Figure 11?

10 A No.

11 Q In Paragraph 113 of your new declaration,
12 Exhibit 1059, could I ask you to turn there,
13 please.

14 A Okay.

15 Q And in the first sentence, you say that,
16 "Dr. Quackenbush complains that my theory is
17 unclear on 'at what step in Linnarsson's method
18 the ligation occurs'"; is that right?

19 A Yes.

20 Q And this paragraph says that "there cannot
21 be any confusion" starting about three lines from
22 the bottom; do you see that?

1 A Yes.

2 Q It says, "There cannot be any confusion on
3 this point because I proposed to carry out the
4 ligation using linker sequences as set forth in
5 prior art such as the Hug reference, which
6 requires a single stranded region to which the
7 linker sequence may hybridize," right?

8 A Yes.

9 Q And then you say that requires a
10 particular sequence timing?

11 A Well, I -- it requires a single stranded
12 region, which would be available after that first
13 step.

14 Q Okay.

15 A But I -- sorry, just to clarify, it
16 doesn't -- it just requires a single stranded
17 step, and so the natural reading is that it be
18 right after that first extension, but that
19 wouldn't preclude -- at any point if you have a
20 single stranded overhang, you can use that linker
21 approach.

22 Q And that's based on the requirements

1 you're laying out for Hug?

2 A It's based upon needing a single stranded
3 linker as disclosed in Hug, yes.

4 Q And a few pages later in your declaration,
5 we get to Paragraph 119, right?

6 A Okay.

7 Q And there you say Hug is just one example
8 of what you had in mind, correct?

9 A Yes, that's right.

10 Q And you say, "Indeed, my prior declaration
11 cited numerous other references providing methods
12 for ligating polynucleotides. Hug is merely one
13 of four exemplary methods for ligation," correct?

14 A That's right.

15 Q And, in fact, there are numerous others
16 you talk about as well?

17 A Yeah, including lots of disclosure from
18 the '981 patent itself about the array of ligation
19 techniques that were available to an artisan and
20 routine and conventional steps.

21 Q Is there a place in your declaration where
22 you analyze how those numerous methods would

1 impact the timing of ligation?

2 A So the key element of timing that I
3 discuss in the original and revised -- and the
4 new dec- -- the reply declaration is with respect
5 to the fact that the reason to add the McCloskey
6 tag is to address the problem of amplification
7 bias, which obviously would require that you do it
8 before amplification.

9 So that's the most important element of
10 timing, and that's what I address in both of these
11 declarations is that it occur before the
12 amplification step.

13 So that would be the only requirement,
14 and, again, that's a reflection of the nature of
15 that tag and what -- the reason that a POSA is
16 adding that tag into the experiment. The reason
17 they're doing that is to reduce amplification
18 bias, so it must occur prior to amplification, but
19 there would be options in terms when exactly it
20 occurred prior to amplification.

21 Q And one of the ways in this declaration,
22 Exhibit 1059, that you narrow that down in

1 Paragraph 113 was to talk about Hug, right?

2 A As -- yes, as an -- as one example among
3 the universe of other -- you know, the many
4 ligation techniques available to a POSA.

5 Q But you didn't do that same analysis like
6 Hug for all the other ways?

7 A Right, I did not go into any extensive
8 detail on the other specific references.

9 Q Now, you say in your new declaration --
10 let's look at Paragraph 122.

11 A Okay.

12 Q Are you with me?

13 Okay. If you turn to Page 83, which is
14 1059.086 in the lower right, still in
15 Paragraph 122, you say, "A POSA would find it
16 obvious and routine to modify and design Hug's
17 linker molecule to hybridize to a non-random
18 portion of McCloskey's barcode," right?

19 A That's right.

20 Q Where in your original declaration,
21 Exhibit 1002, do you explain that a POSA would
22 find it obvious and routine to modify and design

1 Hug's linker molecule to hybridize to a non-random
2 portion of McCloskey's barcode?

3 A So I think this would be captured under
4 the competencies that I set forth for what a POSA
5 would know and be comfortable with, which would
6 include tagging and -- sequencing amplification
7 and using ligation as a way to add tags.

8 So it's -- that's -- to me, that's
9 comfortably inside that definition of the basic
10 skill set that a POSA would have.

11 Q So you didn't explicitly discuss it in
12 Exhibit 1002?

13 A So, again, I would disagree except insofar
14 as the general statement that this clearly, to me,
15 falls within the scope of a competency, which is
16 well defined in my declaration.

17 Q But you didn't say words to this effect.
18 You're saying a person of skill would know it, but
19 you didn't feel the need to talk about it?

20 A I --

21 MR. WALTER: Objection --
22

1 BY THE WITNESS:

2 A -- what level of specificity you're
3 talking about. It's a matter of -- I talk at
4 length about what a POSA would know and the
5 techniques available to them and the fact that
6 ligation is routine and conventional and could be
7 added as a design choice. So there's lots of text
8 to that effect.

9 BY MR. BAUGHMAN:

10 Q Well, do you recall saying that a POSA
11 would have -- would find it obvious and routine to
12 modify and design Hug's linker molecule to
13 hybridize to a non-random portion of a McCloskey's
14 barcode?

15 A I don't believe that specific sentence is
16 there, no.

17 Q How about that a person of skill would
18 have found it obvious to modify Hug's linker
19 molecule to hybridize to Linnarsson's CDS and/or
20 TSO?

21 A Again, I don't think that particular
22 sentence appears.

1 Q And you're saying that these are obvious
2 modifications to Hug, correct?

3 A Yes, these are -- these are obvious ways
4 to achieve ligation of a second tag.

5 Q But what you say is it would have been
6 obvious and routine to modify and design Hug's
7 linker molecule to do these things, right?

8 A Right. In the context of a POSA being
9 motivated to add a second tag to reduce the
10 amplification bias problem proposed by Linnarsson,
11 they would know to use ligation, and that Hug is
12 one possible means of doing that, and that it
13 could be fit into the protocol relatively easily.

14 Q Now, you also say that Hug isn't really a
15 part of your prior art combination anyway, right?

16 A Yes, it's an example method; it's not a
17 document that I, quote/unquote, rely upon as a
18 specific grounds.

19 Q If we look at your Paragraph 119 for a
20 second. Let me know when you're there.

21 A Okay.

22 Q You say, "As state clearly" -- "As stated

1 clearly in my prior declaration, Hug is not" --
2 and you bold and italicize that -- "a reference
3 used as a basis for the grounds of my opinion,"
4 right?

5 A That's right.

6 Q So if it's not a part of the grounds, why
7 are you arguing about making obviousness arguments
8 for changing it?

9 A It's just an example of -- since there
10 seem to be -- in the Quackenbush declaration,
11 there seemed to be some concern about this, and
12 the point was just to provide an example this is
13 one -- merely one option that a POSA would use,
14 that this is all routine and conventional changes,
15 with Hug being one representative example of a
16 method that they could use. Not an exclusive one,
17 not a required one, but certainly one example.

18 Q So you're not making Hug a part of your
19 combination now, are you?

20 A No, it's just an example.

21 MR. BAUGHMAN: Let's take a break.

22 (WHEREUPON, a recess was had.)

1 MR. BAUGHMAN: I pass the witness.

2 EXAMINATION

3 BY MR. WALTER:

4 Q All right, Dr. Cooper. Do you recall you
5 were asked some questions about whether RNA and
6 prokaryotes can have a poly-A tail?

7 A Yes.

8 Q Okay. I marked as Exhibit 1067 a document
9 entitled "Polyadenylation of mRNA Prokaryotes"
10 from 1997.

11 Do you have Exhibit 1067?

12 MR. BAUGHMAN: I'm going to object to the
13 introduction of the document. It's improper.

14 (WHEREUPON, Exhibit No. 1067 was first
15 referenced.)

16 BY MR. WALTER:

17 Q Do you have that, Dr. Cooper?

18 A I do.

19 Q Let's take a look at the abstract. You
20 see where it says, "The 3 prime ends of
21 prokaryotic and eukaryotic of mRNA are
22 polyadenylated but the poly(A) tracks of

1 prokaryotic mRNA are generally shorter, ranging
2 from 15 to 60 adenylate residues and associated
3 with only 2 to 60 percent of the molecules of a
4 given mRNA species.

5 "The sites of polyadenylation of bacterial
6 mRNA are diverse and include the 3 prime ends of
7 primary transcripts, the sites of endonucleolytic
8 processing of the 3 prime untranslated and
9 intercistronic regions, and sites within the
10 coding regions of mRNA degradation products.

11 "The diversity of polyadenylation sites
12 suggests that mRNA polyadenylation of prokaryotes
13 is a relatively indiscriminate process that can
14 occur at all mRNAs 3 prime ends and does not
15 require specific consensus sequences as in
16 eukaryotes."

17 Did you see that?

18 A I do see that.

19 Q Okay. Is this consistent with your
20 understanding of polyadenylation of messenger RNA
21 and prokaryotes that you testified to earlier?

22 A Yes, it is certainly consistent in the

1 sense of it occurs at some level, tends to be less
2 with eukaryotes, but certainly it is a mechanism
3 that is important to at least some bacteria and is
4 part of their mRNA profile.

5 Q And, in your opinion, would someone with
6 skill in the art be able to use the method of
7 Linnarsson with the 15 to 60 adenylate residues
8 that are associated with a fraction of the mRNA
9 molecules in prokaryotic species?

10 A Yes.

11 MR. BAUGHMAN: Objection to form. And
12 scope.

13 BY MR. WALTER:

14 Q Let's take a look at Exhibit 1068. This
15 is a document --

16 MR. BAUGHMAN: I'll object to the
17 introduction of this exhibit well. It's improper.

18 (WHEREUPON, Exhibit No. 1068 was first
19 referenced.)

20 BY MR. WALTER:

21 Q This is a document entitled "RNA
22 Polyadenylation in Prokaryotes Organelles;

1 Different Tails Tell Different Tales."

2 Do you have Exhibit 1068?

3 A Yes.

4 Q And this is from the 2006 time frame.

5 Take a look at the first paragraph, the
6 introduction. It's states, "Polyadenylation is an
7 important post-transcriptional modification of
8 prokaryotic, eukaryotic, and organellar RNA."

9 Do you see that sentence?

10 A I do.

11 Q Okay. What is a post-transcriptional
12 modification?

13 A So that generally refers to, in the
14 process of, sort of, basic functioning of cells,
15 DNA is transcribed into RNA, so the -- an RNA
16 plume race uses DNA as a template and makes an
17 RNA. That process is called transcription. And
18 then once that RNA is made, it can be modified by
19 a variety of molecular mechanisms, including the
20 addition of a poly-A tail or additional
21 nucleotides.

22 So that just means that it doesn't depend

1 on the DNA template inside the genome; it happens
2 after the transcript is initially made, a poly-A
3 is added after that fact.

4 Q And is it your understanding that
5 Exhibit 1068 is describing that taking place in
6 prokaryotes?

7 A Yes. And it is also saying that it is an
8 important mechanism -- important modification that
9 properly serves biological purposes.

10 Q All right. Now, during your direct
11 examination, you were asked a lot about the BtsI
12 enzyme; do you recall that testimony?

13 A I do.

14 Q Is the BtsI enzyme ever mentioned in the
15 Linnarsson reference?

16 A I don't believe so, no.

17 Q What restriction enzyme does the
18 Linnarsson reference mention to your knowledge?

19 A I believe it refers to the BtsCI.

20 Q Now, does the Linnarsson reference ever
21 contemplate using the BtsI restriction enzyme cut
22 site, to your knowledge?

1 A No.

2 MR. BAUGHMAN: Object to the form and
3 basis.

4 BY MR. WALTER:

5 Q Now, you were asked a lot of questions
6 about how in your declaration you state that
7 certain figures in Linnarsson, including, I
8 believe, Figures 3 and 4, don't include any
9 restriction enzyme cut site; do you recall that
10 testimony?

11 A I do.

12 Q Now, when you stated that in your
13 declaration, were you trying to state that the
14 sequences you were pointed to didn't include by
15 happenstance a restriction enzyme cut site for any
16 possible restriction enzyme in the world?

17 A No, that was not --

18 MR. BAUGHMAN: Object to form. And
19 foundation.

20 BY THE WITNESS:

21 A No, that was not the intended meaning.
22

1 BY MR. WALTER:

2 Q Well, what were you trying to say?

3 A That it's different from what's
4 contemplated in Figure 11, and that it doesn't --
5 it lacks the key cut site that Figure 11 discusses
6 as being necessary for releasing from the beads as
7 part of the cleanup.

8 Q What restriction enzyme cut site, if any,
9 is contemplated for use with Figures 3 and 4?

10 A As far as --

11 MR. BAUGHMAN: Object to form.

12 BY THE WITNESS:

13 A As far as I know, that doesn't discuss
14 that at all.

15 BY MR. WALTER:

16 Q Now, you were asked some questions about
17 the use of a linker sequence to do ligation. Do
18 you recall those questions?

19 A Yes.

20 Q Can you please briefly explain how a
21 linker sequence is used to do ligation?

22 A Sure. So the process of a linker is that

1 you have a little overhang of an extra few single
2 stranded nucleotides that you can hybridize then a
3 longer oligonucleotide to, and that facilitates
4 basically and stabilizes that and then allows one
5 to ligate on the additional tag.

6 Q Now, you stated that you can take the
7 longer oligonucleotide and hybridize that to the
8 overhang; do you recall that from just a moment
9 ago?

10 A Yes.

11 Q Okay. And would someone of skill in the
12 art understand that this is what's going to happen
13 simply by virtue of the fact that someone is
14 referring to the use of a linker sequence for
15 ligation?

16 MR. BAUGHMAN: Object to the form. And
17 foundation.

18 BY THE WITNESS:

19 A Yes, I believe so.

20 BY MR. WALTER:

21 Q Now, do you recall what sequences were
22 used in the Hug reference as the hybridization

1 overhangs?

2 A I don't.

3 Q Would someone of -- what would someone of
4 skill in the art understand when it comes to the
5 use of a linker sequence for ligation and whether
6 the specific sequence is used as the hybridization
7 overhangs are required for that method?

8 A They --

9 MR. BAUGHMAN: Object to form -- sorry.
10 You need to let me get my objection first. Sorry.

11 THE WITNESS: Sorry.

12 MR. BAUGHMAN: Objection to the form.
13 Scope. And foundation.

14 BY THE WITNESS:

15 A So the key is that you have to have a
16 region where you can get some hybridization to
17 essentially get that -- the oligo stably bound to
18 your tagged polynucleotide to then facilitate the
19 downstream steps.

20 BY MR. WALTER:

21 Q Would someone of skill in the art
22 understand that for that method, the only

1 sequences that would work would be the Hug
2 sequences that are used?

3 MR. BAUGHMAN: Object to the form. Scope.
4 And foundation.

5 BY THE WITNESS:

6 A No, I don't think so. I think there would
7 be a variety of sequences one could use, with that
8 complementary being an important part, but that
9 encompasses a wide range of possible sequences.

10 BY MR. WALTER:

11 Q And would someone of skill in the art
12 understand that simply by virtue of the fact that
13 someone contemplated using a linker sequence for
14 ligation?

15 MR. BAUGHMAN: Object the form. Scope.
16 And foundation.

17 BY THE WITNESS:

18 A Yes, I believe that those design choices
19 would be comfortably within the competencies of a
20 POSA.

21 MR. WALTER: All right. I don't have any
22 further questions.

1 MR. BAUGHMAN: I have a few questions,
2 Dr. Cooper.

3 FURTHER EXAMINATION

4 BY MR. BAUGHMAN:

5 Q Subject to our objections about
6 Exhibits 1067, 1068, have you seen those documents
7 before today?

8 A I can't remember if I have or not. I may
9 have, but I don't remember specifically.

10 Q When might you have seen them?

11 A I really can't say.

12 Q Did you look for documents like
13 Exhibit 1067 and 1068 in performing the work to
14 render your opinions in the reply declaration,
15 Exhibit 1059?

16 A I don't think so.

17 Q Did you discuss the issues that you have
18 opined about -- excuse me. Strike that.

19 Did you discuss the issues that you
20 testified about in connection with Exhibits 1067
21 and 1068 in either of your declarations?

22 A I don't recall that.

1 Q You don't recall that you did do that?

2 A That's right.

3 MR. BAUGHMAN: Let's take a quick break.

4 (WHEREUPON, a recess was had.)

5 MR. BAUGHMAN: No further questions at
6 this time. Thanks, Dr. Cooper.

7 THE WITNESS: Thanks.

8 MR. WALTER: Court Reporter -- Michelle,
9 Do you need us for anything? Off the record.

10 (WHEREUPON, discussion was had off the
11 record and the deposition was concluded at
12 12:45 p.m. CST)

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ACKNOWLEDGMENT OF DEPONENT

I, Gregory Cooper, Ph.D., do hereby
acknowledge that I have read and examined the
foregoing testimony and the same is a true,
correct, and complete transcription of the
testimony given by me and any corrections appear
on the attached errata sheet signed by me.

(SIGNATURE)

(DATE)

C E R T I F I C A T E O F R E P O R T E R

I, MICHELLE M. YOHLER, a Certified
Shorthand Reporter within and for the County of
Will, State of Illinois, do hereby certify:

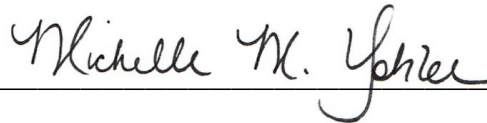
That previous to the commencement of the
examination of the witness, the witness was duly
sworn to testify the whole truth concerning the
matters herein;

That the foregoing deposition transcript
was reported stenographically by me, was
thereafter reduced to typewriting under my
personal direction and constitutes a true record
of the testimony given and the proceedings had;

That the said deposition was taken
remotely before me at the time and place
specified;

That I am not a relative or employee or
attorney or counsel, nor a relative or employee of
such attorney or counsel for any of the parties
hereto, nor interested directly or indirectly in
the outcome of this action.

1 IN WITNESS WHEREOF, I do hereunto set my
2 hand and affix my seal of office at Chicago,
3 Illinois, this 3rd day of May, 2024.

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9 Michelle M. Yohler, CSR, RMR, CRR

10 Certified Shorthand Reporter

11 CSR No.: 84-4531
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Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

161

A			
abbreviated 121:15	across 88:10, 89:3	after 12:4, 41:2,	31:5, 31:17,
abbreviation 97:20	action 159:22	94:11, 102:1,	32:2, 32:3,
able 15:17, 96:1, 148:6	active 108:3, 108:15	103:4, 135:8,	33:20, 34:5,
above 14:13, 63:4, 63:6, 81:1, 81:18, 119:22	actively 65:3	135:9, 136:2,	35:13, 36:2,
absence 73:3	actual 59:20, 109:16	136:3, 138:12,	47:14, 47:17,
absent 65:9, 67:18, 68:14, 68:20, 120:11, 126:12	actually 21:5, 45:9, 62:13, 64:22, 114:17, 116:4, 125:18, 129:10, 130:2	138:18, 150:2, 150:3	48:9, 54:3,
abstract 72:19, 134:22, 146:19	add 53:20, 109:9, 109:22, 110:18, 140:5, 142:7, 144:9	again 13:6, 17:7, 17:10, 22:9, 22:18, 24:15, 25:16, 26:16, 27:18, 33:5, 35:12, 36:6, 40:8, 41:16, 42:3, 42:20, 43:12, 44:4, 45:4, 49:9, 49:20, 52:3, 53:2, 54:13, 57:10, 59:17, 60:20, 65:5, 65:12, 70:4, 71:15, 72:3, 74:1, 78:5, 78:16, 78:22, 80:18, 84:14, 86:8, 95:3, 95:21, 101:12, 106:2, 108:14, 110:15, 110:18, 113:8, 117:4, 122:3, 124:20, 125:3, 125:8, 125:17, 128:3, 128:5, 129:1, 131:16, 134:3, 136:16, 140:14, 142:13, 143:21	64:3, 64:8, 64:13, 64:16, 65:3, 65:5, 65:8, 74:11, 74:15, 75:16, 90:18, 90:22, 91:8, 91:20, 92:14, 94:18, 95:18, 96:5, 96:8, 96:12, 97:9, 102:22, 103:2, 105:20, 107:16, 107:19, 111:14, 116:3, 120:20, 127:21, 131:10
abundant 73:5	added 66:11, 82:3, 82:14, 83:7, 143:7, 150:3	ago 11:12, 67:15, 153:9	agreeing 11:11
access 7:20, 8:3	adding 140:16	agree 19:4, 24:20, 25:4, 26:21, 28:18, 29:6, 29:14, 30:19,	ahead 8:19, 14:1, 56:1, 56:5, 56:9, 56:10, 56:15, 81:18, 99:9, 119:2
accidentally 59:22	addition 149:20		all 7:4, 13:9, 16:12, 19:9, 21:8, 22:11, 23:16, 25:4, 25:7, 26:17, 26:18, 28:16, 31:4, 31:6, 31:15, 31:18, 31:19, 31:22, 32:1, 32:2, 32:11, 32:18, 33:11, 33:15, 33:17, 33:19, 34:7, 34:11, 34:13, 34:21, 35:4, 35:7, 35:8, 35:16,
accommodate 98:3, 99:18	additional 30:20, 32:16, 96:1, 107:7, 111:17, 113:4, 149:20, 153:5		
accommodated 101:6	address 69:6, 69:18, 78:2, 140:6, 140:10		
accompanied 77:5	addressed 13:5, 37:14, 71:18		
accomplished 102:7, 102:19, 103:1	addressing 10:11		
account 51:6	adenines 63:7		
accounted 122:20	adenylate 147:2, 148:7		
achieve 144:4	affix 160:2		
acids 20:12, 21:9			
acknowledge 158:3			
acknowledgment 158:1			

Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

162

35:18, 36:5, 36:7, 43:15, 47:22, 50:5, 52:5, 52:9, 53:9, 57:12, 70:9, 71:12, 74:10, 74:17, 75:12, 75:13, 85:18, 86:14, 92:10, 92:16, 101:16, 108:21, 116:19, 122:6, 122:18, 126:9, 128:12, 130:13, 137:5, 141:6, 145:14, 146:4, 147:14, 150:10, 152:14, 155:21 allele 38:18 allowed 10:7, 10:15, 10:20 allows 153:4 almost 110:16 alone 54:1 alphabetical 60:22 already 28:14, 110:1, 113:5, 113:6, 117:21 also 4:10, 14:17, 20:14, 20:19, 38:10, 38:13, 72:1, 75:2, 75:13, 80:14, 81:7, 83:13, 83:15, 91:15, 95:18, 97:9, 99:3, 108:2, 109:6, 119:13, 124:19, 126:12, 128:4, 133:12,	144:14, 150:7 alteration 6:8 always 102:13, 108:5, 108:18, 113:16 among 59:14, 141:2 amongst 77:19 amount 75:9 amplification 37:19, 44:22, 51:10, 88:2, 89:15, 122:14, 140:6, 140:8, 140:12, 140:17, 140:18, 140:20, 142:6, 144:10 amplification-bi- as-producing 57:1 amplify 35:18 amplifying 34:13 analogous 19:21, 20:7, 22:5, 22:7, 26:3, 26:22, 27:7, 28:7, 28:16 analysis 19:19, 20:17, 22:6, 23:6, 23:13, 25:6, 25:7, 25:19, 28:2, 33:22, 38:11, 133:9, 141:5 analyze 34:7, 34:11, 34:20, 35:4, 35:15, 139:22 analyzing 20:12, 20:21, 21:10	another 10:21, 28:16, 54:21, 54:22, 86:13, 86:14, 126:20, 128:1 answer 35:12, 66:22, 69:13, 76:21 answered 25:2, 26:5, 26:14, 28:11, 53:17, 54:9, 55:3, 59:8 answering 48:3 any 8:8, 10:10, 10:17, 12:1, 12:5, 12:14, 15:13, 17:14, 19:1, 19:3, 21:4, 22:1, 22:13, 23:2, 30:5, 30:12, 30:20, 32:9, 32:16, 39:3, 41:14, 43:10, 44:11, 47:2, 48:16, 51:6, 52:18, 53:14, 54:6, 55:15, 69:1, 75:1, 75:16, 76:7, 92:6, 94:3, 95:5, 100:12, 104:4, 118:2, 118:11, 119:2, 119:12, 120:4, 120:9, 120:15, 121:22, 125:13, 125:20, 130:14, 131:2, 132:17, 132:18, 134:6, 137:7, 137:21, 138:2, 138:19, 141:7, 151:8, 151:15, 152:8, 155:21, 158:6,	159:20 anything 8:4, 12:10, 54:7, 76:2, 109:10, 157:9 anyway 144:15 anywhere 40:6, 84:18 apart 52:13 apologize 56:6 appeal 1:2 appear 27:20, 80:16, 158:6 appears 27:7, 38:11, 76:20, 95:19, 97:19, 143:22 apples 129:1 applicable 71:3 application 34:10, 58:8 applications 34:12 applied 36:4 applies 108:21 apply 92:10 approach 117:13, 117:19, 127:17, 138:21 approaches 6:17, 35:9, 68:12 apps 8:8 arbitrary 96:1 area 66:12
--	--	--	---

aren't 31:13, 71:2, 82:18 argue 104:18, 118:11, 119:13 argued 51:18, 60:12 arguing 22:22, 47:4, 74:3, 86:18, 88:21, 145:7 argument 28:6, 28:8, 47:21, 48:7, 115:19, 118:13 arguments 9:5, 145:7 arise 39:3 arising 38:18 around 11:22, 12:2, 103:17, 111:5 array 139:18 art 22:5, 22:7, 45:22, 73:16, 104:19, 136:10, 138:5, 144:15, 148:6, 153:12, 154:4, 154:21, 155:11 article 6:11, 6:16, 67:1, 68:2, 68:3, 69:2, 91:8 artisan 101:18, 139:19 asked 25:1, 26:4, 26:13, 28:10, 53:16, 54:8, 55:2, 90:10, 146:5, 150:11, 151:5, 152:16	asking 21:17, 56:3, 118:17, 124:9, 124:10 aspect 12:14 aspects 87:20, 127:19, 130:9, 130:12, 132:21, 133:5 assert 23:14 assertion 15:19 associated 147:2, 148:8 assume 8:2, 8:7, 11:2, 66:22, 130:3 assumed 110:1 assure 75:17 attached 5:10, 77:15, 158:7 attention 72:18, 73:8 attorney 159:19, 159:20 attorneys 7:4 audio 59:7 authors 69:9, 76:8, 134:7, 136:20 available 8:5, 120:21, 138:12, 139:19, 141:4, 143:5 avenue 4:5 average 98:22 aware 73:16, 73:19, 74:11, 121:5,	136:9 B back 29:1, 83:18, 94:8, 99:20, 103:20, 105:2, 111:4, 113:17 background 72:21 bacteria 64:3, 64:10, 65:1, 65:6, 65:13, 69:20, 69:21, 70:2, 70:5, 70:7, 70:9, 70:10, 71:5, 71:11, 71:20, 73:21, 74:3, 74:7, 74:17, 74:19, 75:2, 75:8, 75:18, 76:2, 148:3 bacterial 6:12, 73:2, 73:11, 75:14, 147:5 bacteriologist 64:11 bar 79:12, 79:16 barcode 37:21, 38:14, 38:17, 38:21, 39:8, 40:1, 40:14, 40:22, 41:6, 41:9, 41:17, 42:2, 42:5, 42:10, 42:13, 43:5, 43:11, 44:2, 44:3, 44:7, 45:1, 46:17, 47:8, 49:8, 49:12, 50:16, 50:17, 50:19, 50:21, 51:4,	51:13, 52:5, 52:14, 53:10, 53:21, 54:14, 54:17, 55:7, 56:22, 57:1, 57:9, 141:18, 142:2, 143:14 barcodes 37:1, 37:12, 39:2, 39:12, 41:21, 42:17, 42:19, 42:22, 43:16, 44:6, 44:12, 47:10, 49:4, 51:5, 52:9, 53:6, 53:20, 54:2, 55:17, 57:4 barcoding 44:22, 51:9 base 99:1, 101:6, 122:20, 123:12, 129:18, 129:21 based 63:1, 125:12, 138:22, 139:2 bases 54:7, 99:6, 124:20 basic 142:9, 149:14 basically 153:4 basis 23:1, 129:5, 129:15, 145:3, 151:3 batch 38:16, 43:4, 44:1, 44:18, 50:1, 53:21, 54:16 bates 59:19 baughman 3:11, 3:12, 4:4, 5:4, 5:6,
---	--	---	--

Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

164

7:6, 7:16, 8:18, 9:6, 9:13, 10:5, 12:20, 13:20, 13:22, 14:4, 15:21, 17:3, 17:16, 22:21, 24:6, 24:19, 25:10, 26:1, 26:10, 26:20, 28:17, 35:10, 50:8, 51:11, 54:5, 55:13, 56:6, 56:11, 57:7, 65:22, 66:4, 67:14, 72:9, 77:10, 78:20, 79:15, 83:1, 85:13, 86:16, 90:2, 91:7, 91:19, 93:3, 97:12, 97:16, 100:15, 109:19, 112:13, 120:19, 128:16, 133:16, 133:21, 134:5, 134:21, 143:9, 145:21, 146:1, 146:12, 148:11, 148:16, 151:2, 151:18, 152:11, 153:16, 154:9, 154:12, 155:3, 155:15, 156:1, 156:4, 157:3, 157:5 baughman@groombr- idgewu 3:16 bead 96:21, 97:6 beads 128:21, 152:6 because 12:9, 32:3, 32:14, 32:15, 69:9, 71:19, 78:2, 78:18, 92:6, 108:17,	113:3, 116:17, 123:4, 126:10, 129:17, 138:3 been 7:13, 7:18, 11:12, 12:3, 12:8, 12:9, 14:13, 37:10, 45:20, 54:19, 66:1, 67:8, 121:11, 136:10, 144:5 before 1:2, 2:2, 7:3, 11:11, 11:14, 11:20, 12:4, 12:6, 39:16, 67:2, 69:16, 70:15, 75:19, 84:5, 84:8, 97:13, 102:4, 120:8, 121:12, 133:22, 136:10, 136:22, 137:7, 140:8, 140:11, 156:7, 159:16 beginning 7:19, 106:8 begins 28:19, 102:18 behalf 3:2, 3:10, 4:2 behave 127:12 behaviors 33:4 being 88:15, 96:1, 102:7, 121:15, 125:17, 144:8, 145:15, 152:6, 155:8 believe 10:9, 10:10, 10:17, 11:1, 11:15, 14:19, 17:7, 20:3, 28:14, 29:1,	39:14, 42:14, 47:5, 47:11, 48:22, 57:21, 58:19, 58:21, 67:15, 70:1, 70:5, 70:11, 71:1, 75:21, 76:3, 76:20, 82:21, 91:5, 97:19, 109:4, 143:15, 150:16, 150:19, 151:8, 153:19, 155:18 believed 70:18 bell 67:13, 76:11, 121:11 below 62:5, 62:6, 62:7, 62:8, 63:19, 63:20, 82:2, 82:9, 82:14 beneath 62:12 besides 44:14, 53:15, 55:16, 122:11 better 29:3 between 73:20, 74:14, 86:1, 133:4 beyond 48:18, 75:21, 78:16 bias 37:19, 44:22, 51:10, 140:7, 140:18, 144:10 bio" 79:22 biolabs 121:3, 121:15, 134:9, 136:17, 136:19 biological 150:9	biology 64:9 biosciences 1:4 biotin 76:16, 76:20, 77:7, 77:13, 77:15, 78:1, 78:6, 78:8, 78:12, 78:17, 78:18, 80:3, 80:5, 80:19, 81:11, 83:19, 83:22, 84:2, 89:11, 96:15, 115:20, 116:1, 119:13, 119:17, 127:15, 128:5, 128:21, 128:22, 130:20, 131:2, 131:5, 131:7, 131:11, 131:12, 131:21 biotins 131:4 bits 88:13, 88:21, 89:3 black 79:12, 79:16 blanket 30:21 block 36:19, 36:20, 105:10, 105:13, 105:16, 105:17, 105:20, 106:1, 106:11, 111:8, 112:2, 114:6, 114:8, 114:9, 114:11 bmc 6:11, 72:10 board 1:2, 49:16 bold 145:2 both 35:8, 39:5,
--	--	--	---

42:20, 43:20, 44:6, 54:2, 62:11, 62:14, 62:16, 85:7, 90:3, 90:11, 109:7, 125:1, 140:10 bottom 94:14, 97:5, 105:10, 135:10, 136:4, 137:22 bound 65:10, 67:19, 68:15, 68:21, 154:17 box 79:22 boxed 62:5, 62:8, 63:18 brad 4:11 break 66:1, 66:11, 75:3, 97:13, 145:21, 157:3 bridges 80:13 brief 12:13, 12:15 briefly 152:20 bring 14:12 broadly 104:3 bs 13:10 bts 120:13, 123:22, 124:6 btsci 120:14, 124:1, 127:8, 150:19 btssi 6:10, 124:4, 124:12, 125:1, 127:8, 135:2,	135:7, 136:1, 150:11, 150:14, 150:21 built 92:8 bunch 7:18 C calculating 39:11, 39:19, 50:20 california 3:6 call 55:5, 55:14, 55:15, 72:18, 120:13 called 7:13, 11:2, 43:3, 85:8, 85:9, 88:22, 96:13, 121:9, 121:13, 149:17 calling 73:8, 87:6 can't 11:11, 13:9, 22:13, 29:22, 58:20, 60:20, 61:1, 64:10, 67:11, 70:14, 70:17, 106:17, 126:15, 128:20, 128:21, 156:8, 156:11 cannot 126:7, 137:20, 138:2 capture 68:13, 96:14, 96:17, 96:21, 97:6, 118:6, 118:10, 126:9, 126:11, 127:17 captured 142:3 capturing 73:4, 117:18	carries 127:18 carry 138:3 case 1:12, 36:12, 63:1, 87:18, 100:11, 108:20, 126:7 catalogue 125:11 caught 60:2 caveat 118:1 cdna 21:1, 32:5, 59:3, 61:20, 61:21, 62:9, 62:18, 63:13, 82:3, 82:14, 83:7, 100:16, 100:17, 100:18, 100:21, 101:9, 106:12, 106:16, 107:2, 107:3, 107:9, 107:17, 108:5, 108:18, 109:3, 109:15, 109:16, 110:1, 110:5, 110:11, 110:14, 110:22, 111:13, 111:15, 111:16, 111:20, 113:3 cdnas 101:2, 101:5, 108:10 cds 59:2, 61:19, 62:7, 62:20, 62:22, 63:4, 63:18, 84:9, 84:12, 85:9, 85:11, 86:10, 87:7, 95:22, 96:3, 96:4, 116:1, 117:17,	118:3, 119:1, 120:1, 143:19 cdss 86:9, 87:3, 88:5, 90:6, 90:22, 91:3, 92:4, 92:6, 131:5 cell 6:16, 20:17, 28:20, 29:7, 29:16, 29:21, 30:9, 31:3, 31:7, 32:15, 32:19, 34:8, 34:21, 35:16, 36:5, 38:18, 44:17, 45:13, 45:14, 45:17, 46:22, 48:21, 56:22, 63:19, 66:6, 69:2, 73:5, 82:10, 84:12, 107:5, 107:11, 107:12, 122:13, 122:14, 122:21 cells 16:20, 20:13, 20:22, 21:9, 28:3, 29:11, 29:13, 30:17, 73:1, 107:6, 107:14, 149:14 certain 16:8, 48:8, 60:20, 87:20, 115:21, 151:7 certainly 13:8, 13:20, 30:11, 31:2, 46:13, 59:6, 60:15, 71:18, 77:8, 85:9, 94:20, 101:4, 101:20, 102:9, 103:6, 109:21, 110:10, 145:17,
---	---	---	--

147:22, 148:2 certified 2:3, 159:3, 160:10 certify 159:5 cetera 21:10, 28:3, 31:13, 32:12, 41:3, 44:9, 45:7, 85:21, 86:14, 87:8, 88:3, 88:6, 88:18, 89:15, 91:5 cg 124:2 challenging 73:2 change 10:7, 10:10, 68:18, 76:5 changes 128:19, 145:14 changing 145:8 characterization 29:3 characterized 33:15 chart 132:13, 132:21 check 58:18 chicago 160:2 choice 143:7 choices 52:8, 53:11, 155:18 choose 55:6 chose 51:12, 111:1, 114:11 chromosome 108:13	citation 41:11, 42:1, 44:14, 44:20, 45:7, 50:3, 105:11 citations 106:3, 113:20 cite 38:10, 38:13, 38:19, 39:20, 40:8, 40:11, 40:14, 43:12, 50:12, 50:13, 50:15, 83:12, 104:8, 132:7 cited 39:14, 70:13, 77:12, 82:6, 99:8, 139:11 citing 47:9, 105:4, 130:7 claim 13:5, 13:8, 13:11, 14:13, 15:1, 15:9, 15:12, 15:19, 16:3, 16:19, 17:2, 17:9, 28:4, 46:1, 48:6, 48:7, 50:5, 51:18, 51:21, 51:22, 52:11, 52:20, 53:4, 59:12, 59:15, 60:13, 60:17, 61:3, 61:5, 62:2, 64:1, 77:18, 83:6, 84:17, 85:5, 86:15, 86:18, 86:20, 87:19, 87:21, 88:12, 88:14, 88:19, 88:20, 89:8, 89:11, 89:22, 114:7, 131:22, 132:7,	132:13, 132:14, 132:16, 132:17, 132:18, 132:22, 133:2, 133:4, 133:14 claims 12:17, 13:2, 16:7, 17:14, 20:10, 27:11, 27:19, 46:7, 48:1, 89:14, 104:16, 106:4, 131:22, 132:12, 133:7, 133:11 clarification 79:14 clarify 18:7, 138:15 clean 8:3 cleaner 105:18 cleanup 152:7 clear 23:19, 25:21, 26:8, 26:19, 28:5, 28:14, 38:8, 41:4, 41:12, 42:20, 44:10, 47:6, 47:11, 49:7, 50:4, 55:11, 55:18, 57:21, 78:5, 85:2, 86:12, 87:10 clearly 21:11, 34:16, 43:19, 51:8, 51:15, 52:6, 57:15, 96:3, 110:20, 115:22, 126:13, 126:21, 127:5, 130:20, 131:4, 132:5, 133:3, 142:14, 144:22, 145:1 cleavage 135:6, 135:22	cloned 107:3, 107:18 closed 59:22 coaching 56:13 coding 147:10 coining 109:1 colleague 66:13 collection 107:3, 107:18 colon 18:17 column 93:11, 93:20, 94:11, 94:12, 95:9, 95:11, 97:2, 103:14, 105:4, 105:6, 105:21, 106:21, 109:9, 135:5, 135:16, 135:17, 135:18 com 3:8, 3:16, 4:8 combination 47:4, 50:7, 51:18, 52:19, 53:8, 57:10, 104:19, 144:15, 145:19 combine 37:17, 46:6, 53:4, 57:4, 85:14, 89:3 combined 23:16, 44:19 combining 56:21 come 83:18 comes 154:4 comfortable 48:3, 65:11,
---	---	---	--

69:9, 69:14, 75:22, 101:14, 142:5 comfortably 142:9, 155:19 commencement 159:6 comment 12:5, 12:14 common 88:1, 88:5 company 134:19 compared 88:15 compatible 77:8 competencies 45:21, 142:4, 155:19 competency 142:15 complains 137:16 complementary 107:3, 107:18, 110:14, 155:8 complete 158:5 compliance 16:17 component 96:16, 125:16 components 47:12 comprise 111:20 comprises 31:6, 32:18, 43:4, 43:5, 43:17, 44:1, 44:2, 45:1, 46:17, 49:6, 51:13, 52:14 comprising 14:9, 18:17, 82:10, 112:19 conceptually 45:12, 46:20	concern 145:11 concerning 159:8 concerns 115:19 concluded 157:11 conducting 23:5 confident 65:21, 122:5, 129:12 confuse 18:6 confused 124:5 confusion 137:21, 138:2 connection 71:11, 133:4, 156:20 connects 21:6, 132:21 consensus 147:15 consider 49:16, 69:21, 92:16, 108:1 considered 22:5, 66:9 considering 27:10 consistent 147:19, 147:22 constitute 107:4 constitutes 159:13 constraints 91:5 contain 73:11, 119:2, 120:4, 120:9, 129:10 contained 73:17, 100:17 contains 107:11, 119:11,	119:16 contemplate 42:21, 57:2, 103:6, 150:21 contemplated 43:20, 50:6, 123:3, 152:4, 152:9, 155:13 contemplating 126:8 context 40:18, 40:21, 43:14, 45:5, 46:3, 49:21, 51:15, 53:5, 57:20, 62:19, 82:6, 82:22, 83:3, 84:6, 84:14, 90:4, 90:11, 108:7, 110:19, 111:17, 114:9, 126:13, 130:10, 133:9, 144:8 contextual 16:5 contiguous 108:12 continue 63:16, 82:12 continued 3:22, 5:22 conventional 49:10, 139:20, 143:6, 145:14 cooper 1:16, 2:1, 5:3, 5:11, 5:15, 7:12, 7:17, 14:5, 26:21, 28:18, 35:13, 36:8, 47:17, 56:1, 56:16, 58:7, 58:15, 59:1, 64:3, 66:5, 67:16, 76:8, 76:13, 97:17, 104:14,	105:19, 113:10, 133:22, 134:6, 146:4, 146:17, 156:2, 157:6, 158:2 copies 8:3, 38:19 copy 59:22, 72:2 core 91:4 corner 68:2 correct 8:6, 8:13, 9:12, 13:7, 15:1, 15:2, 22:15, 24:1, 24:9, 26:12, 27:15, 28:9, 37:7, 46:16, 50:14, 50:22, 54:22, 62:15, 62:18, 67:17, 68:19, 74:20, 77:13, 77:18, 79:5, 79:10, 80:20, 81:9, 81:13, 81:16, 81:20, 82:4, 84:3, 87:1, 90:4, 94:1, 98:19, 100:5, 102:8, 102:22, 103:18, 104:6, 105:5, 106:13, 106:14, 107:6, 107:14, 111:16, 111:22, 113:14, 113:15, 113:21, 114:2, 114:13, 115:17, 117:14, 118:7, 118:12, 120:5, 123:15, 125:1, 125:14, 125:21, 134:1, 134:10, 135:3, 136:4, 139:8,
--	---	--	--

139:13, 144:2, 158:5 corrections 158:6 correspond 38:7 corresponding 17:5, 85:19 cost-effective 6:12 could 10:2, 12:8, 20:4, 28:6, 30:14, 31:12, 31:14, 33:6, 33:12, 39:1, 43:17, 45:12, 45:18, 46:19, 49:5, 49:13, 52:7, 53:1, 54:15, 54:21, 58:2, 58:21, 59:16, 64:11, 66:14, 75:2, 92:7, 92:13, 93:7, 98:3, 98:17, 99:18, 101:19, 101:20, 103:3, 103:10, 103:13, 103:14, 109:5, 113:13, 124:14, 128:14, 130:19, 137:12, 143:6, 144:13, 145:16, 155:7 counsel 56:11, 66:13, 72:2, 159:19, 159:20 county 159:4 couple 106:10 court 157:8 coverage 60:13 covering 106:3	creating 102:1 critical 127:15 crr 1:22, 2:3, 160:9 csr 1:22, 2:3, 2:4, 160:9, 160:11 cst 1:18, 157:12 curiosity 76:7 currently 38:22, 51:7 cut 118:12, 119:3, 119:13, 119:18, 120:5, 120:9, 120:10, 120:12, 120:15, 120:22, 121:6, 121:19, 122:2, 122:3, 122:7, 122:9, 123:1, 123:18, 124:3, 124:7, 124:12, 124:14, 124:22, 125:6, 125:10, 125:14, 125:17, 125:21, 126:2, 126:10, 126:18, 127:1, 127:3, 127:11, 127:14, 127:20, 128:1, 128:17, 129:3, 129:10, 129:19, 129:20, 129:22, 130:2, 130:4, 130:6, 130:16, 130:21, 131:21, 137:6, 137:7, 150:21, 151:9, 151:15, 152:5, 152:8 cuts 135:7, 136:1 cutting 132:2	cytoplasm 31:13 cytoplasmic 33:5 D date 158:10 day 12:3, 12:4, 160:3 dec 140:4 declarations 70:22, 71:2, 140:11, 156:21 deep 70:9 define 124:6, 129:17 defined 40:14, 55:8, 60:22, 62:20, 64:14, 111:15, 111:16, 142:16 defines 38:14, 51:8, 103:17, 106:15 definition 22:6, 38:20, 39:5, 39:20, 39:22, 40:4, 40:5, 40:8, 40:16, 41:9, 41:10, 41:17, 42:1, 43:13, 44:7, 45:8, 47:9, 49:3, 50:10, 50:13, 50:17, 50:19, 51:3, 52:20, 53:7, 55:9, 106:18, 109:7, 110:21, 142:9 definitions 54:13 degradation 65:10, 65:16,	67:19, 68:15, 68:21, 147:10 degree 87:22, 117:6 demonstrated 63:4 depend 100:21, 101:7, 101:16, 149:22 depending 31:11, 37:1, 37:12, 41:21, 42:22, 44:13 depends 101:12 depict 62:5 depicts 63:18, 82:9 depletion 6:15 deponent 158:1 deposition 1:16, 2:1, 157:11, 159:10, 159:15 derek 3:3, 3:8, 7:9, 13:22 describe 18:12, 30:20, 32:16, 48:16, 87:16, 127:2, 129:12 described 37:21, 63:11, 90:7, 104:2, 106:12, 111:13, 112:2 describes 20:9, 20:11, 20:16, 33:13, 35:3, 36:3, 50:21 describing 19:8, 71:11, 130:6, 150:5
--	---	--	--

description 63:11, 71:16, 86:4, 96:3 design 42:4, 49:9, 52:7, 53:11, 91:4, 141:16, 141:22, 143:7, 143:12, 144:6, 155:18 designated 43:18, 45:12, 46:20 designation 129:22 designed 36:4 designing 34:14 detail 41:11, 141:8 detailed 19:19, 132:13 details 22:10, 101:17, 116:19, 124:13, 127:18 determining 39:2, 51:5 dictates 17:2 difference 74:13, 86:1, 89:19 different 6:4, 33:8, 33:9, 36:9, 37:1, 37:12, 38:18, 41:6, 41:21, 44:12, 47:18, 47:22, 73:20, 74:5, 74:9, 85:8, 85:10, 85:12, 85:15, 86:10, 87:3, 87:17, 88:8, 88:9, 88:10, 89:1,	89:3, 89:8, 89:20, 123:5, 124:9, 124:14, 125:10, 126:18, 126:21, 127:1, 127:3, 127:9, 127:10, 127:11, 128:6, 128:17, 130:9, 149:1, 152:3 differential 33:3, 33:4 differentiate 16:20 differently 30:15, 33:6, 127:12 difficult 116:15 digests 135:2 digging 69:5, 69:12, 69:14, 69:16 direct 150:10 directed 21:11 direction 159:13 directly 159:21 directs 59:3, 62:8, 63:13 disagree 25:8, 25:16, 26:7, 28:13, 32:13, 32:21, 34:18, 41:8, 49:19, 142:13 disagreed 10:12 disclose 117:17, 125:18 disclosed 19:1, 19:5, 52:10, 57:3,	83:5, 84:9, 85:3, 116:19, 124:15, 126:14, 139:3 discloses 14:8, 33:1, 43:3, 44:1, 84:20, 96:13, 103:3, 104:3, 104:19, 117:12, 118:6 disclosing 33:15, 130:9, 132:5 disclosure 31:21, 56:19, 84:16, 87:10, 91:18, 116:18, 117:7, 125:9, 132:15, 132:18, 132:22, 133:2, 139:17 disclosures 51:22, 57:13, 76:15, 77:18, 77:20, 84:19, 88:9, 115:22 discuss 38:1, 39:11, 39:18, 70:21, 78:18, 117:5, 140:3, 142:11, 152:13, 156:17, 156:19 discussed 26:17, 27:8, 71:1, 91:21, 113:9, 113:12, 116:7, 117:21, 119:21, 131:15 discusses 47:18, 91:9, 152:5 discussing 48:17, 81:19, 104:18 discussion 41:12, 44:11,	45:5, 53:5, 61:16, 63:17, 79:4, 81:7, 81:22, 92:6, 103:9, 104:15, 114:6, 117:6, 157:10 discussions 92:10 distinct 117:13 distinguish 38:17, 45:16, 46:21, 48:19, 52:17 dive 70:9 diverse 147:6 diversity 42:7, 51:5, 147:11 dna 20:17, 98:17, 100:5, 100:12, 100:13, 102:20, 107:3, 107:18, 108:13, 109:22, 110:14, 149:15, 149:16, 150:1 document 12:6, 27:18, 46:11, 58:16, 67:9, 70:20, 83:16, 92:15, 112:7, 118:4, 144:17, 146:8, 146:13, 148:15, 148:21 documents 13:19, 43:21, 156:6, 156:12 doing 8:22, 17:8, 71:13, 77:22, 96:17, 129:1, 132:4, 140:17, 144:12
---	--	---	---

dominated 98:6 done 32:10, 45:18, 47:3, 49:5, 54:15, 103:3, 113:6, 130:15 doubt 69:1, 69:3 down 68:6, 80:11, 119:8, 119:19, 119:20, 140:22 download 7:21, 13:19, 66:12, 72:2 downstream 154:19 dozen 98:18 dozens 98:8, 99:5 dr 7:17, 9:4, 9:7, 9:16, 10:13, 10:20, 14:5, 26:21, 28:18, 35:13, 36:8, 47:17, 56:1, 56:16, 58:7, 58:15, 59:1, 64:3, 66:5, 67:16, 76:8, 76:13, 97:17, 104:14, 105:19, 113:10, 115:4, 116:3, 117:3, 133:22, 134:6, 137:16, 146:4, 146:17, 156:2, 157:6 due 73:2 duly 7:11, 7:13, 159:7 during 61:20, 66:11,	73:13, 82:3, 82:15, 83:8, 150:10 E each 13:2, 19:7, 23:22, 28:20, 29:7, 29:15, 29:20, 30:8, 31:7, 32:15, 36:12, 87:20, 88:12, 88:19, 89:1, 118:11, 132:13, 132:15 earlier 67:8, 113:10, 113:12, 147:21 early 11:11 easily 73:12, 144:13 echo 81:4 effect 30:22, 142:17, 143:8 effectively 100:7 efficient 6:11, 73:4 either 54:1, 70:21, 71:6, 117:3, 156:21 element 13:2, 14:13, 16:3, 38:16, 46:8, 48:17, 49:12, 53:5, 140:2, 140:9 elements 12:17, 13:11, 16:6, 16:19, 33:2, 34:3, 48:6, 84:15, 85:4, 85:18, 85:19, 86:18,	88:13, 88:19, 89:9, 122:19, 123:4, 132:16, 133:1, 133:2, 133:4, 133:13, 133:15 elimination 30:20, 32:17 else 8:4, 8:9, 48:14, 54:7 elsewhere 42:3, 125:4 emailed 66:12, 66:13 embodiment 131:20 embodiments 31:2, 31:9, 31:19, 32:1, 33:17, 33:18, 34:16, 36:7, 48:9, 57:14, 59:6, 59:10, 59:11, 59:14, 62:21, 77:4, 77:8, 78:6, 78:8, 85:15, 89:20, 96:10, 117:12, 119:12, 126:9, 128:13, 131:6 employee 159:18, 159:19 empowered 45:21 enables 73:4 encompass 10:2, 33:9, 109:4 encompasses 35:8, 109:7, 155:9 end 19:12, 73:12, 88:3, 96:21, 97:6, 99:14,	112:3, 112:4, 123:11 endeavor 19:21, 21:8, 21:12, 21:16, 21:21, 22:1, 22:3, 22:8, 22:12, 22:15, 22:20, 23:7, 23:10, 23:15, 23:18, 23:22, 24:9, 24:12, 24:22, 25:8, 25:12, 25:21, 26:9 endonuclease 6:10, 135:1 endonucleolytic 147:7 ends 65:14, 105:10, 146:20, 147:6, 147:14 england 121:2, 121:14, 134:9, 136:17, 136:19 enough 16:16, 23:14 enrich 73:12 enrichment 73:4 entail 34:12 entire 19:8, 27:10, 44:4, 55:5, 55:14, 70:8 entitled 92:15, 146:9, 148:21 entity 134:12 enzyme 118:12, 119:2, 119:13, 119:18, 120:5, 120:9,
--	--	---	---

121:6, 121:19, 122:2, 122:7, 122:8, 123:18, 123:20, 124:3, 124:11, 124:15, 124:22, 125:3, 125:10, 125:14, 125:21, 126:2, 126:10, 126:14, 126:18, 126:22, 127:3, 127:14, 128:1, 128:17, 129:3, 129:10, 134:16, 136:14, 137:6, 150:12, 150:14, 150:17, 150:21, 151:9, 151:15, 151:16, 152:8 enzymes 127:10, 134:20 equate 27:3 equates 21:5 errata 158:7 especially 28:1, 110:19 essentially 37:17, 42:21, 43:18, 53:11, 92:14, 109:8, 154:17 et 21:10, 28:3, 31:13, 32:12, 41:3, 44:9, 45:7, 85:21, 86:14, 87:8, 88:3, 88:6, 88:18, 89:15, 91:5 eukaryote-focusi- ng 68:11 eukaryotes 73:10, 74:6,	74:15, 75:6, 147:16, 148:2 eukaryotic 64:16, 65:3, 73:1, 73:21, 73:22, 75:12, 146:21, 149:8 even 11:11, 23:5, 53:20, 57:17, 125:10 ever 18:6, 29:19, 42:12, 71:10, 121:2, 150:14, 150:20 every 19:1, 19:3, 38:4, 38:5, 122:20, 129:17, 129:21 everything 32:7, 48:10, 48:11, 69:4 everywhere 108:21 evidence 13:4, 22:19, 23:17, 25:17, 25:20, 26:18, 48:5, 48:12, 60:16, 64:19, 70:11, 70:12, 70:15, 77:3, 77:20, 85:6, 88:14 exact 14:20 exactly 13:10, 40:14, 90:16, 92:1, 106:18, 116:6, 116:9, 121:13, 140:19 examination 7:15, 146:2, 150:11, 156:3, 159:7	examined 7:14, 158:3 example 14:21, 16:19, 28:2, 31:11, 32:5, 33:5, 34:14, 37:16, 38:3, 38:15, 42:19, 47:8, 49:20, 50:1, 53:3, 53:14, 54:6, 54:15, 54:18, 54:21, 54:22, 57:15, 57:16, 57:17, 62:4, 63:17, 63:18, 71:16, 77:5, 86:13, 86:14, 87:7, 88:1, 89:11, 90:4, 90:12, 90:13, 91:21, 93:13, 94:1, 94:8, 94:19, 95:19, 96:6, 96:9, 96:12, 97:10, 98:21, 99:4, 101:2, 108:1, 110:4, 110:12, 112:11, 117:16, 117:22, 118:6, 119:20, 128:14, 130:6, 130:7, 130:10, 130:13, 130:14, 130:20, 131:10, 131:12, 131:14, 131:18, 131:22, 132:4, 137:8, 139:7, 141:2, 144:16, 145:9, 145:12, 145:15, 145:17, 145:20 examples 65:1, 83:4, 86:10, 87:3, 87:11, 87:17, 93:15, 94:3,	101:5, 117:1 except 8:9, 65:9, 67:18, 68:15, 68:20, 133:12, 142:13 excepted 10:3 excerpt 62:13, 80:18, 81:12 exclude 33:18, 71:20, 94:6 excludes 48:8 excluding 54:17, 78:1, 87:14 exclusion 32:9, 36:6, 102:10 exclusionary 35:5 exclusive 57:18, 145:16 excuse 156:18 exemplary 51:16, 51:20, 52:1, 119:1, 119:11, 120:1, 139:13 exhibit 8:13, 8:14, 9:8, 9:9, 9:16, 9:18, 9:19, 12:21, 13:15, 14:6, 14:17, 14:22, 17:18, 18:1, 18:8, 18:12, 19:12, 19:18, 20:5, 21:15, 21:18, 22:13, 23:2, 24:1, 25:13, 27:1, 27:14, 28:8, 36:13,
--	---	--	---

36:16, 37:10, 39:11, 41:20, 42:13, 50:11, 58:3, 58:11, 58:17, 59:17, 66:15, 66:16, 67:6, 69:16, 69:17, 71:7, 71:14, 72:1, 72:4, 72:5, 73:18, 75:19, 75:20, 76:1, 76:4, 76:14, 78:11, 78:21, 92:20, 93:1, 97:18, 98:11, 102:15, 103:13, 103:21, 104:12, 105:21, 106:20, 111:5, 113:17, 114:15, 114:19, 115:9, 117:9, 122:17, 123:6, 133:19, 134:1, 134:4, 135:14, 136:11, 137:12, 140:22, 141:21, 142:12, 146:8, 146:11, 146:14, 148:14, 148:17, 148:18, 149:2, 150:5, 156:13, 156:15 exhibits 5:10, 7:21, 66:11, 99:7, 156:6, 156:20 exist 70:5, 70:11, 74:10, 74:16 expand 37:1, 37:12, 54:1 expanding 41:6, 41:15, 41:20, 44:12 experience 70:19, 72:13	experiment 37:3, 37:13, 39:9, 41:22, 43:1, 44:14, 47:13, 53:12, 58:1, 101:8, 101:13, 101:17, 140:16 experimental 52:7 expert 6:6 explain 20:6, 79:17, 85:14, 88:9, 89:2, 141:21, 152:20 explained 25:5, 25:6 explanation 24:11, 40:22 explanations 19:20, 23:21, 24:8 explicit 28:8 explicitly 49:22, 57:5, 142:11 express 56:19 expressed 107:11, 107:13 expression 20:22, 33:22, 34:2, 34:4 expressly 50:6, 57:3 extension 138:18 extensive 141:7 extent 12:10, 16:8, 32:4, 35:22, 48:7, 74:3, 77:3, 89:19, 91:2, 92:2,	115:18, 123:1, 130:17, 132:20 extra 53:22, 153:1 extreme 74:15 F facilitate 154:18 facilitates 153:3 fact 44:16, 47:7, 47:8, 55:8, 77:11, 83:11, 107:22, 114:1, 116:17, 122:11, 125:13, 129:20, 139:15, 140:5, 143:5, 150:3, 153:13, 155:12 fair 67:22, 69:15, 75:11, 75:13, 91:16 fall 31:20, 52:9 falls 142:15 familiar 66:5, 72:10, 121:14, 134:13 far 152:10, 152:13 fate 69:19 fates 70:10 fault 135:18 features 88:4, 89:21, 92:12 feel 8:19, 18:6, 26:18, 44:9, 48:2, 78:19,	86:12, 142:19 felt 56:4, 75:22, 117:6 few 61:11, 98:18, 101:6, 119:19, 139:4, 153:1, 156:1 field 19:21, 21:12, 21:15, 21:21, 22:1, 22:3, 22:7, 22:11, 22:15, 22:20, 23:7, 23:9, 23:15, 23:18, 23:22, 24:9, 24:12, 24:22, 25:8, 25:12, 25:20, 26:9, 134:15 fifth 4:5, 68:6 figure 18:12, 18:16, 18:22, 29:1, 62:11, 62:12, 62:16, 63:11, 63:18, 71:16, 77:4, 77:6, 79:12, 79:16, 79:21, 80:6, 80:8, 80:18, 81:11, 82:3, 82:6, 82:9, 82:14, 82:22, 83:10, 83:12, 83:20, 83:21, 84:5, 84:12, 86:2, 86:3, 87:5, 88:13, 89:2, 90:5, 90:14, 91:9, 91:10, 92:9, 92:11, 94:16, 94:19, 95:16, 95:18, 96:5,
---	--	--	---

Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

173

103:4, 104:6, 116:14, 116:20, 116:21, 117:13, 117:19, 118:22, 119:22, 120:11, 120:12, 122:4, 122:9, 122:19, 123:7, 123:12, 123:21, 124:19, 125:19, 126:3, 126:4, 126:9, 126:12, 126:14, 126:16, 126:17, 126:22, 127:15, 127:17, 127:19, 128:2, 128:4, 128:8, 128:9, 130:1, 131:1, 131:9, 131:17, 137:9, 152:4, 152:5 figures 62:4, 62:14, 62:16, 62:19, 63:4, 77:6, 77:12, 77:14, 78:17, 79:9, 80:15, 81:8, 81:16, 83:14, 89:17, 90:3, 90:7, 90:10, 90:17, 91:2, 91:13, 91:16, 91:20, 92:2, 92:5, 92:16, 115:5, 115:17, 115:22, 116:4, 116:7, 117:16, 117:21, 118:9, 120:8, 120:13, 122:1, 125:1, 125:14, 129:9, 129:22, 130:7, 130:9, 130:12, 131:3, 131:13, 137:2, 151:7, 151:8, 152:9 filed 11:14, 11:18,	11:20, 11:22, 12:3, 12:6 filled 39:4 filtration 30:20, 32:17 find 13:12, 13:21, 14:20, 22:13, 23:8, 27:21, 36:22, 58:20, 58:22, 118:20, 121:19, 141:15, 141:22, 143:11 fine 18:5 finish 55:22, 56:1, 56:5, 56:8, 56:9, 56:10, 56:15, 127:16 finished 113:10 first 5:10, 7:13, 8:14, 9:9, 9:19, 16:20, 38:5, 45:12, 61:19, 66:16, 68:11, 72:5, 72:19, 73:9, 73:10, 93:1, 95:15, 99:22, 106:10, 112:15, 133:19, 134:22, 137:15, 138:12, 138:18, 146:14, 148:18, 149:5, 154:10 fit 47:13, 57:22, 86:11, 144:13 five 119:8 flavor 92:7 focus 116:13, 122:3, 125:17	focused 10:11, 21:8, 27:11, 27:18, 34:2, 34:3, 87:22, 122:10, 133:2 focusing 132:11 folks 12:12 following 18:17, 126:11 follows 7:14, 23:8 footnote 58:9 foregoing 158:4, 159:10 form 9:1, 15:10, 16:14, 22:16, 24:2, 24:13, 25:2, 25:14, 26:4, 26:13, 28:11, 34:22, 49:17, 51:1, 53:16, 54:9, 55:3, 56:13, 76:18, 78:14, 82:19, 84:22, 86:6, 89:5, 90:20, 91:11, 100:9, 109:12, 112:6, 112:16, 120:16, 128:10, 134:17, 148:11, 151:2, 151:18, 152:11, 153:16, 154:9, 154:12, 155:3, 155:15 formalities 7:19 formality 8:7 formatting 13:9 formed 127:22	formula 39:2, 51:4 forth 28:7, 82:10, 117:19, 134:16, 138:4, 142:4 forward 61:12 found 88:22, 107:10, 143:18 foundation 151:19, 153:17, 154:13, 155:4, 155:16 four 139:13 fraction 15:20, 148:8 fragment 100:5, 100:12, 100:18, 101:14, 101:21, 108:2, 108:9, 108:11, 108:18, 110:2, 113:2, 113:14, 127:17 fragment's 100:12 fragmentation 96:13, 102:11, 102:19, 103:7, 104:5, 107:20, 108:3, 108:15, 113:4, 113:7, 114:2, 114:3, 117:18, 118:6, 118:10, 126:8, 129:4, 132:1 fragmented 108:6 fragmenting 101:11, 102:8, 103:3, 112:2, 112:10, 112:22 fragments 98:3, 99:17, 100:8, 100:18,
---	--	---	--

101:9, 107:4, 107:18, 107:21, 109:5, 109:8, 110:4, 110:7, 110:11, 111:1, 111:14, 111:16, 126:11 frame 149:4 free 8:19, 18:7 frequency 75:17 fulfill 89:8 fulfills 87:20 full 10:3, 50:17, 95:15 full-length 100:17, 108:2, 108:10, 109:5 fully 107:10, 107:22, 110:20 function 50:21, 85:11, 129:17, 131:5, 131:6, 131:9 functional 129:21 functionality 62:17, 64:22 functioning 149:14 functions 56:21, 91:1, 91:4 fundamentally 73:20, 74:5 further 63:10, 80:11, 101:10, 103:3, 111:20, 112:1, 112:14, 112:18, 113:14, 120:3, 155:22, 156:3,	157:5 G gave 24:7, 98:21 gcagtg 123:15, 124:3, 124:11, 124:20, 135:2, 135:7, 136:1, 136:14 gcatg 124:8 gene 20:22, 33:22, 34:2, 34:3 gene-family-spec- ific 34:15 general 19:5, 20:10, 20:15, 20:21, 21:12, 30:11, 30:16, 33:2, 39:6, 42:5, 53:7, 70:18, 74:12, 75:5, 75:6, 75:7, 90:5, 91:15, 92:11, 98:5, 108:9, 109:7, 110:22, 113:3, 130:18, 130:22, 142:14 generally 18:16, 20:11, 29:12, 34:2, 46:12, 66:9, 69:4, 147:1, 149:13 generate 61:20 generating 60:7, 61:7, 62:2, 62:18 generation 97:18, 98:1, 99:15, 112:5 generic 100:13, 108:16,	116:18 genes 107:12, 107:13 genome 150:1 genomics 1:9, 6:11, 72:11 germane 78:3 getting 101:15 ggatg 124:7 give 13:12, 14:21, 53:14, 59:22, 99:3 given 36:5, 39:3, 45:21, 51:6, 53:9, 62:13, 75:2, 105:8, 110:19, 137:8, 147:4, 158:6, 159:14 giving 49:19, 53:2, 57:14, 69:16, 91:2, 92:7, 110:6 go 8:19, 14:1, 28:22, 39:16, 41:2, 50:2, 56:1, 56:5, 56:9, 56:15, 62:4, 65:22, 78:21, 94:8, 97:14, 114:20, 133:16, 141:7 goals 101:12 goes 63:14, 107:7, 107:9, 111:19 going 17:17, 35:12,	36:15, 67:4, 67:7, 72:3, 72:18, 111:4, 114:19, 146:12, 153:12 gone 28:14, 54:12 good 7:17, 8:11, 59:21, 97:12 gotshal 3:4, 7:10 governing 23:13 great 8:1, 38:1, 97:22, 99:13 greatly 100:21 green 62:8, 63:6, 63:19, 63:20, 79:21 gregory 1:16, 2:1, 5:3, 5:11, 5:15, 7:12, 158:2 groombridge 3:12, 4:4, 7:8 grounds 144:18, 145:3, 145:6 guanine 123:13 guanines 122:12 guess 27:5, 35:11, 48:14, 49:19, 55:5, 71:21, 72:15, 89:9 guessing 67:6 H hand 160:2 handle 33:6
--	--	--	--

happen 31:10, 123:2, 153:12 happening 48:14 happens 31:12, 70:8, 125:11, 150:1 happenstance 129:14, 129:16, 151:15 hard 13:21, 76:21, 136:19 heading 60:6, 72:21, 81:2, 86:5, 93:13, 96:19, 97:5 hear 85:22, 87:2 heard 121:2 heavily 115:19 held 2:1 helpful 28:22 helps 19:12 here 10:15, 14:12, 16:6, 30:1, 32:2, 34:18, 36:13, 41:4, 43:15, 43:20, 44:5, 48:1, 49:15, 54:4, 57:3, 57:19, 60:19, 86:18, 87:6, 87:7, 104:18, 106:6, 111:2, 118:20, 119:2, 123:11, 124:6, 129:1, 129:9, 129:20 here's 86:13, 86:14,	130:2 hereby 158:2, 159:5 herein 7:13, 106:12, 111:13, 159:9 hereto 159:21 hereunto 160:1 hi 66:5 highlighted 62:6, 63:6, 63:19, 130:5 hint 105:9 hold 13:18, 55:21, 67:4, 76:18, 115:12 homework 136:21 hoping 101:18 hour 66:1 however 61:5, 68:13, 73:1 hug 138:5, 139:1, 139:3, 139:7, 139:12, 141:1, 141:6, 144:2, 144:11, 144:14, 145:1, 145:15, 145:18, 153:22, 155:1 hug's 141:16, 142:1, 143:12, 143:18, 144:6 huge 75:9 human 6:17 hundred 98:19, 101:6	hundreds 98:8, 99:6 hybridization 153:22, 154:6, 154:16 hybridize 63:7, 138:7, 141:17, 142:1, 143:13, 143:19, 153:2, 153:7 hybridizing 59:4 I identified 15:5, 15:15, 104:21 identify 7:4, 15:18, 45:14, 120:22 ignore 115:21 ignores 57:12, 115:5, 115:17, 116:17 iis 6:9, 135:1 illinois 159:5, 160:3 illumina 99:4 illustrate 91:14 illustrations 77:20 imagine 80:8 immediately 84:4, 84:8 impact 140:1 implement 31:14 implementations 45:20 implementing 47:3 implication 107:20	implicit 15:16 implied 49:21 imply 96:17, 108:3, 108:15 implying 35:22 important 38:9, 41:2, 46:12, 62:22, 78:19, 90:18, 91:1, 91:6, 91:17, 140:9, 148:3, 149:7, 150:8, 155:8 imposed 16:18 improper 146:13, 148:17 inc 1:4, 1:9 include 31:15, 31:18, 32:6, 33:11, 33:17, 33:18, 34:10, 77:13, 79:9, 81:16, 83:12, 104:5, 108:9, 119:12, 119:17, 142:6, 147:6, 151:8, 151:14 included 23:21, 77:12, 80:7, 80:19, 81:8, 81:12, 83:20, 84:2, 106:2, 111:9 includes 39:21, 39:22, 40:16, 42:1, 50:13, 51:14, 59:2, 63:5, 72:16, 79:22, 84:2, 103:9, 129:14, 131:12
---	---	--	--

including 19:20, 20:16, 29:13, 32:11, 32:12, 48:18, 80:6, 110:5, 126:14, 127:19, 139:17, 149:19, 151:7 inclusion 32:9, 78:17 inclusive 110:21 incompatible 31:1, 117:18, 118:10 incorporate 39:8 incorrect 116:16 indeed 139:10 indicate 116:1 indicates 110:7, 113:1 indicating 81:2 indicative 112:10 indirectly 12:8, 159:21 indiscriminantly 29:15, 29:18, 29:20, 30:4, 30:10, 30:18, 31:4, 32:14 indiscriminate 147:13 individual 19:7, 28:21, 29:8, 47:12, 48:6 inform 16:7, 91:9, 118:4 information 100:4, 107:8 informative 95:7, 131:17	informing 118:2 initially 150:2 input 6:13, 29:4, 32:6, 102:20 inputs 100:8 insert 96:1 inside 94:19, 95:19, 120:13, 131:13, 142:9, 150:1 insofar 142:13 instead 84:19 instruct 39:7, 95:5 instruction 91:15 intended 129:19, 130:4, 151:21 inter 5:13 intercistronic 147:9 interested 159:21 interpret 92:17 interrupting 56:7 intrinsically 47:10 introduced 67:8, 91:21, 131:13 introduction 67:5, 67:9, 72:4, 106:7, 134:4, 146:13, 148:17, 149:6 investigation 75:17, 121:22,	137:4 ipr 1:12, 10:4, 11:3, 11:4, 11:17, 36:9, 76:15 issue 37:14, 37:20, 90:1 issues 156:17, 156:19 italicize 145:2 itself 102:7, 130:20, 139:18 J job 1:20 john 6:6 josh 7:7 joshua 4:3, 4:8 journal 66:6, 66:8, 66:10, 72:16, 72:17 jump 56:2, 111:5 jumping 99:9, 119:1 K keep 50:9, 56:2 key 140:2, 152:5, 154:15 kinds 33:8, 33:9, 35:8 know 7:17, 10:3, 12:1, 12:4, 12:10, 12:13,	14:1, 14:16, 30:14, 58:14, 60:14, 64:12, 65:18, 65:19, 70:5, 70:14, 71:9, 76:7, 76:9, 76:10, 93:8, 94:3, 101:16, 102:3, 102:16, 118:15, 121:9, 122:18, 123:9, 123:17, 124:2, 124:11, 124:17, 128:15, 129:8, 136:18, 141:3, 142:5, 142:18, 143:4, 144:11, 144:20, 152:13 knowledge 91:3, 150:18, 150:22 known 70:6, 70:18 L label 77:15, 78:17 lack 68:7, 126:1, 127:14 lacks 118:11, 128:4, 152:5 language 15:13, 16:18, 28:4, 29:1, 48:8, 50:2, 50:6, 50:9, 51:18, 51:22, 54:17, 59:12, 59:15, 61:3, 61:5, 77:18, 78:4, 83:6, 84:17, 85:5, 86:15, 87:9, 87:19, 87:21, 88:15, 88:20,
--	---	--	---

89:8, 95:1, 95:21, 132:22 large 74:6, 74:8 larger 54:2 last 42:8, 52:13, 73:8 later 110:19, 139:4 lay 12:16 laying 139:1 learn 121:17 least 33:16, 34:9, 57:2, 57:4, 57:12, 92:7, 96:16, 110:14, 132:10, 148:3 left 68:2, 68:6, 135:18 legal 23:13 length 15:20, 38:1, 39:1, 39:3, 41:18, 42:12, 42:22, 44:8, 45:5, 47:12, 51:4, 51:6, 52:8, 54:2, 54:14, 55:1, 55:8, 99:1, 101:4, 119:21, 143:4 lengths 37:1, 37:12, 41:6, 41:21, 42:16, 43:11, 44:6, 44:13, 44:18, 49:8 less 148:1	let's 65:22, 78:21, 82:7, 92:20, 97:14, 104:11, 106:19, 114:17, 117:8, 122:15, 123:6, 133:16, 141:10, 145:21, 146:19, 148:14, 157:3 lettering 61:2 letters 79:22 level 143:2, 148:1 library 21:1, 100:16, 100:22, 101:9, 102:1, 102:6, 102:11, 102:12, 102:18, 106:12, 106:16, 107:2, 107:17, 110:5, 111:13, 111:15, 111:20, 111:21, 112:4, 113:3 library's 110:10 ligate 153:5 ligating 139:12 ligation 137:18, 138:4, 139:13, 139:18, 140:1, 141:4, 142:7, 143:6, 144:4, 144:11, 152:17, 152:21, 153:15, 154:5, 155:14 limit 56:12, 115:20 limitation 14:17, 15:9, 15:17, 16:17, 52:21, 60:13,	60:17, 60:18, 61:16, 62:2, 63:22, 79:5, 81:3, 81:8, 81:20, 82:1, 83:3, 86:17, 104:15, 106:3, 114:7, 114:12, 116:14 limitations 13:6, 16:10, 50:5, 88:10, 88:12, 90:1 limited 50:20, 99:16 limits 109:17 line 99:14, 103:17, 109:9, 119:20, 135:1, 135:19 lines 85:5, 105:5, 105:21, 106:21, 117:11, 117:12, 119:8, 119:19, 137:21 link 7:21, 72:2 linker 138:4, 138:7, 138:20, 139:3, 141:17, 142:1, 143:12, 143:18, 144:7, 152:17, 152:21, 152:22, 153:14, 154:5, 155:13 linnarsson's 28:19, 31:17, 31:21, 33:20, 34:6, 34:20, 35:15, 45:13, 59:2, 63:11, 76:15, 77:17, 82:8, 87:6, 90:4, 90:11, 117:22, 118:5,	118:22, 119:22, 125:9, 132:22, 137:17, 143:19 list 18:18 listed 128:9 literal 27:19 literature 69:8 little 80:10, 119:2, 120:3, 124:5, 153:1 lloréns-rico 66:19 llp 3:4, 3:12, 4:4 locations 40:13, 48:12, 96:2 logic 85:20 logically 23:8 long 17:1, 101:10, 105:13, 108:12, 113:13 longer 153:3, 153:7 look 13:17, 14:19, 17:17, 19:10, 26:16, 26:17, 34:17, 35:6, 35:8, 35:18, 36:7, 36:15, 37:16, 42:8, 47:7, 58:2, 70:15, 71:14, 71:15, 71:22, 87:2, 92:15, 96:4, 103:11, 103:14, 104:11, 105:9, 106:19, 116:8, 117:8,
--	--	---	---

120:15, 122:15, 123:6, 123:12, 124:19, 126:4, 137:3, 137:5, 137:7, 141:10, 144:19, 146:19, 148:14, 149:5, 156:12 looked 11:9, 11:10, 12:2, 86:22, 113:21, 120:10 looking 20:4, 21:8, 38:4, 77:6, 80:10, 97:1, 98:10, 101:2, 102:14, 105:7, 106:10, 111:8, 114:14, 118:14, 120:7, 132:10 looks 9:12, 15:2, 96:15, 105:6 lost 59:7, 135:12 lot 7:19, 72:16, 134:19, 150:11, 151:5 lots 22:9, 22:18, 25:17, 25:19, 28:3, 32:4, 40:21, 48:5, 48:11, 48:15, 54:13, 69:7, 91:13, 130:11, 133:1, 139:17, 143:7 low 6:13, 98:8, 99:6 lower 60:3, 68:2, 79:8, 97:3, 101:3, 141:14 lysed 30:17	lysis 31:11 M made 136:10, 149:18, 150:2 main 121:8 make 7:20, 12:5, 28:6, 30:21, 116:15 makes 28:4, 149:16 making 18:21, 42:20, 63:7, 78:11, 145:7, 145:18 manges 3:4, 7:10 many 26:11, 34:2, 34:11, 38:11, 39:2, 49:14, 68:11, 93:15, 103:6, 141:3 map 50:5, 52:11, 59:12, 59:15, 83:5, 85:18, 86:15, 88:14, 89:3, 89:17, 132:17 mapped 85:18, 133:14 mapping 46:1, 48:1, 49:11, 51:17, 51:20, 52:1, 60:12, 60:18, 62:1, 63:22, 76:14, 77:17, 84:15, 84:18, 84:20, 85:15, 87:18, 88:13, 88:18, 133:11 maps 48:6, 48:10,	78:4, 85:4, 133:12 marked 65:15, 146:8 matter 30:11, 95:19, 102:10, 143:3 matters 159:9 maybe 16:22, 71:8, 128:15, 128:17 mccloskey 13:3, 19:20, 20:16, 21:20, 21:22, 22:10, 23:9, 27:3, 28:16, 37:11, 37:18, 37:21, 38:4, 38:10, 38:14, 38:16, 39:6, 39:21, 40:4, 40:10, 40:15, 41:17, 42:17, 42:21, 43:3, 43:22, 44:15, 44:18, 44:21, 46:6, 49:2, 49:4, 49:13, 50:3, 50:7, 50:18, 50:20, 50:22, 51:21, 52:5, 52:10, 53:3, 55:7, 55:9, 56:22, 58:8, 140:5 mccloskey's 36:22, 37:11, 41:10, 47:9, 52:14, 141:18, 142:2, 143:13 mean 12:8, 18:1, 29:17, 30:4, 34:1, 56:7, 69:3, 87:5, 90:5, 91:13,	94:20, 100:11, 109:5, 130:17, 132:3 meaning 98:16, 111:14, 117:2, 151:21 meaningless 109:9, 109:21 means 77:9, 109:6, 135:7, 136:1, 144:12, 149:22 meant 92:18, 95:7 measure 17:15, 38:9 mechanism 148:2, 150:8 mechanisms 149:19 mechanistic 70:7 meet 15:8, 52:19, 52:20 mention 22:4, 27:16, 57:19, 71:11, 80:5, 83:9, 94:18, 129:13, 150:18 mentioned 130:1, 150:14 mentions 26:22, 95:6, 114:3 merely 54:18, 139:12, 145:13 mes 64:21 messages 8:9 messenger 147:20 method 14:8, 18:16, 20:17, 20:21,
---	--	---	--

28:19, 30:15, 31:14, 31:18, 33:7, 33:8, 33:20, 34:7, 34:20, 35:3, 35:15, 36:4, 36:22, 37:11, 92:13, 106:11, 111:12, 126:14, 128:6, 129:4, 130:18, 130:22, 131:19, 137:17, 144:16, 145:16, 148:6, 154:7, 154:22 methods 19:6, 19:9, 20:12, 31:1, 31:20, 33:10, 35:6, 71:2, 71:3, 92:18, 139:11, 139:13, 139:22 michelle 1:22, 2:2, 157:8, 159:3, 160:9 microbiome 6:17 mid 88:17 midway 119:15 might 28:22, 35:3, 46:15, 47:3, 49:8, 49:9, 49:14, 55:6, 67:1, 75:5, 87:11, 90:9, 91:9, 96:4, 98:11, 101:10, 101:14, 116:11, 156:10 mind 98:12, 131:1, 139:8 mine 46:12	minutes 97:13 mischaracterizes 112:7 misheard 90:9 missed 52:22, 59:8 modification 149:7, 149:12, 150:8 modifications 78:12, 144:2 modified 149:18 modify 141:16, 141:22, 143:12, 143:18, 144:6 mole 108:13 molecular 149:19 molecule 63:8, 78:18, 100:14, 101:15, 108:14, 109:15, 128:22, 141:17, 142:1, 143:12, 143:19, 144:7 molecules 31:7, 32:18, 34:8, 34:21, 35:16, 36:5, 73:5, 73:13, 107:21, 109:17, 110:6, 110:8, 110:16, 110:21, 110:22, 147:3, 148:9 moment 67:13, 67:15, 114:21, 153:8 months 11:12 more 8:7, 10:11, 20:13, 41:11,	69:5, 69:11, 69:14, 73:2, 112:2, 113:3, 130:18, 130:22, 133:2, 136:20 morning 7:17 most 64:10, 98:6, 140:9 motivated 144:9 motivation 37:17, 46:5, 46:12 moving 81:2 mrna 5:19, 6:13, 28:19, 28:21, 29:7, 29:8, 29:11, 29:15, 29:19, 30:8, 30:17, 31:6, 31:7, 32:14, 32:17, 32:18, 34:7, 34:21, 35:16, 36:5, 59:4, 62:5, 63:8, 64:17, 65:4, 65:8, 67:17, 68:13, 68:19, 70:8, 73:1, 73:4, 73:11, 107:10, 108:1, 108:2, 110:20, 146:9, 146:21, 147:1, 147:4, 147:6, 147:10, 147:12, 148:4, 148:8 mrna" 68:7 mrnas 29:13, 31:4, 34:11, 34:13, 35:19, 65:1, 65:9, 65:13,	67:18, 68:13, 68:14, 68:20, 69:19, 70:1, 74:6, 108:10, 147:14 much 15:7, 17:10 multi 32:11 multiple 11:10, 39:14, 40:13, 77:2, 83:4, 84:15, 84:16, 84:19, 85:5, 110:5, 110:11, 114:9 multiplicity 32:11 must 140:18 myself 118:20 N names 76:11 narrow 17:14, 140:22 native 59:20 natural 138:17 nature 38:1, 39:6, 41:8, 42:4, 44:4, 74:13, 109:17, 140:14 near 19:12, 97:5 neb 121:15, 125:11 nebcutter 121:10, 121:18 necessarily 16:21, 19:8, 31:1, 31:8, 31:15, 31:19, 33:18, 48:8,
---	---	---	---

48:9, 48:13, 65:20, 69:3, 71:19, 94:6, 100:20, 113:7, 113:16, 123:3, 130:8, 130:13 necessary 56:14, 152:6 need 16:9, 16:10, 17:4, 49:16, 56:4, 100:18, 101:10, 110:17, 110:18, 113:14, 113:16, 142:19, 154:10, 157:9 needed 126:11 needing 139:2 needs 15:8, 37:2, 37:13, 41:22, 42:22, 44:14, 47:13, 57:22 never 50:10, 58:15, 74:2 new 4:6, 10:15, 10:17, 17:21, 18:3, 67:6, 103:21, 121:2, 121:14, 134:9, 136:17, 136:19, 137:11, 140:4, 141:9 next 45:9, 45:15, 46:20, 52:16, 63:10, 80:22, 81:18, 82:12, 95:9, 95:10, 96:20, 97:18, 98:1, 99:15, 105:9, 112:4 ngs 97:20, 98:15,	98:22, 99:4, 100:7, 100:19, 101:11, 113:13 nick 96:21, 97:6 nomenclature 60:21 non-random 141:17, 142:1, 143:13 none 76:11 nonexclusive 57:16 noon 97:13 nope 121:21 notes 8:4, 37:19 nothing 41:5, 71:5, 77:7, 89:10 notice 2:2 noun 108:16, 110:9 nuclear 33:6 nuclei 64:10 nucleic 20:12, 21:9 nucleotide 54:16, 125:2 nucleotides 38:22, 43:5, 43:6, 44:2, 44:3, 45:2, 45:13, 45:15, 46:16, 46:17, 46:20, 48:19, 51:13, 52:15, 52:16, 53:15, 53:22, 55:1, 57:8, 135:8, 136:2, 149:21, 153:2	nucleus 31:12, 64:6 number 13:12, 18:8, 38:7, 39:12, 40:15, 43:13, 50:16, 55:16, 55:20, 57:8, 57:19, 58:20, 59:19, 59:21, 60:22, 68:2, 102:2 numbered 14:13, 61:6, 97:3 numbering 13:7, 79:7 numbers 13:8, 27:19, 55:6, 55:15, 60:3 numerosity 110:3, 110:8 numerous 119:11, 119:17, 139:11, 139:15, 139:22 nw 3:13 O object 67:5, 67:8, 72:3, 76:18, 134:3, 146:12, 148:16, 151:2, 151:18, 152:11, 153:16, 154:9, 155:3, 155:15 objected 10:12 objection 9:1, 12:19, 15:10, 16:14, 17:11, 22:16, 24:2, 24:13, 25:1, 25:14, 26:4, 26:13,	28:10, 34:22, 49:17, 51:1, 53:16, 54:8, 55:2, 78:14, 82:19, 84:22, 86:6, 89:5, 90:20, 91:11, 100:9, 109:12, 112:6, 112:16, 120:16, 128:10, 134:17, 142:21, 148:11, 154:10, 154:12 objections 56:13, 156:5 obtain 15:4, 15:14, 29:5, 29:11, 99:16, 104:20, 111:21, 112:3 obtaining 29:2 obvious 36:22, 37:11, 46:7, 46:8, 53:4, 141:16, 141:22, 143:11, 143:18, 144:1, 144:3, 144:6 obviously 16:10, 140:7 obviousness 19:19, 22:5, 23:5, 25:6, 25:19, 145:7 occur 95:6, 140:11, 140:18, 147:14 occurred 140:20 occurs 45:3, 148:1 occurs'" 137:18 office 1:1, 160:2 often 64:14, 77:2,
--	--	--	---

102:19, 103:1 oh 8:17, 11:9, 90:13, 115:10, 135:17 okay 8:12, 8:21, 13:16, 14:3, 17:20, 18:2, 18:9, 19:15, 36:18, 56:18, 57:8, 58:4, 58:6, 61:11, 64:7, 65:22, 66:2, 68:5, 72:20, 79:21, 80:12, 83:17, 93:7, 93:9, 93:19, 94:10, 100:1, 100:7, 102:17, 103:15, 104:1, 104:13, 105:12, 106:6, 106:10, 111:7, 112:14, 114:16, 114:18, 114:21, 114:22, 115:12, 116:22, 117:10, 118:14, 118:18, 119:7, 123:8, 123:10, 129:8, 135:17, 137:14, 138:14, 139:6, 141:11, 141:13, 144:21, 146:8, 147:19, 149:11, 153:11 oligo 154:17 oligo-dt 62:7, 63:5, 63:12, 79:19 oligonucleotide 153:3, 153:7 once 149:18 one 8:7, 13:12,	28:16, 31:11, 34:10, 35:3, 35:17, 37:20, 45:17, 46:22, 48:4, 48:13, 48:20, 49:8, 49:20, 51:14, 51:20, 53:3, 54:14, 54:18, 55:6, 58:13, 65:11, 65:18, 65:19, 67:11, 70:13, 75:4, 76:5, 84:8, 86:17, 86:20, 87:11, 91:14, 92:7, 93:5, 96:16, 103:6, 103:7, 103:11, 108:12, 112:11, 112:20, 114:3, 114:8, 114:21, 118:21, 119:20, 121:8, 122:8, 122:10, 123:17, 124:17, 125:5, 125:16, 126:3, 126:20, 127:22, 128:20, 129:8, 129:14, 130:19, 131:2, 131:18, 132:15, 136:13, 136:20, 139:7, 139:12, 140:21, 141:2, 144:12, 145:13, 145:15, 145:16, 145:17, 153:4, 155:7 one's 122:21 ones 94:7, 137:8 only 8:2, 22:4, 26:21, 34:17, 35:19, 36:1, 41:19, 54:4, 57:17, 57:19,	60:15, 64:16, 65:3, 65:15, 91:21, 98:3, 98:17, 99:5, 100:3, 100:7, 101:15, 107:11, 122:11, 128:8, 140:13, 147:3, 154:22 open 8:8, 8:19, 13:14, 31:3, 66:14, 92:20 open-ended 48:2, 96:3 opened 30:17 opening 9:17, 10:4 opined 120:8, 156:18 opining 12:17 opinion 14:8, 15:7, 18:21, 45:10, 59:1, 69:16, 118:3, 125:12, 125:16, 127:22, 128:7, 129:6, 136:11, 145:3, 148:5 opinions 9:17, 10:8, 10:10, 10:15, 10:18, 70:16, 73:18, 75:19, 156:14 opposed 110:11 optimize 53:12, 101:22 optimized 57:22 option 145:13 optional 89:21, 92:13	optionality 48:15, 48:16 options 140:19 oranges 129:1 order 98:8, 99:20 ordinarily 64:17 organellar 149:8 organelles 6:3, 148:22 organisms 64:17, 64:20, 65:3, 71:4, 73:22 organization 95:19 organizational 94:21 origin 45:14 original 9:17, 10:8, 10:10, 11:5, 12:22, 13:1, 13:15, 19:17, 20:5, 20:20, 21:18, 37:9, 37:15, 37:22, 38:12, 39:5, 58:16, 59:17, 60:11, 61:3, 71:10, 76:13, 76:21, 78:10, 79:4, 79:7, 102:14, 104:8, 104:12, 140:3, 141:20 originally 61:6 other 10:2, 13:4, 16:6, 16:9, 16:18, 17:8, 23:22, 34:11,
---	---	---	---

35:5, 36:6, 39:17, 43:11, 45:16, 45:19, 46:10, 46:15, 46:21, 47:2, 48:4, 48:8, 48:16, 48:20, 49:14, 50:14, 52:1, 52:18, 53:14, 54:6, 54:18, 55:15, 57:9, 57:13, 58:13, 65:12, 65:18, 65:19, 67:11, 75:4, 76:5, 77:19, 86:21, 89:1, 89:14, 89:20, 94:3, 94:7, 95:6, 96:10, 103:12, 118:4, 120:15, 123:17, 124:17, 125:6, 127:19, 127:22, 128:15, 128:19, 129:9, 129:18, 130:11, 130:14, 130:19, 136:14, 137:4, 139:11, 141:3, 141:6, 141:8 others 52:17, 139:15 out 12:16, 23:3, 55:5, 55:14, 55:15, 69:8, 76:7, 89:2, 99:20, 101:15, 101:18, 121:5, 121:19, 129:20, 138:3, 139:1 outcome 159:22 outlined 85:21 outlines 110:3	over 10:15, 54:12, 56:3 overall 41:12, 85:20, 86:11, 90:8, 91:6, 91:17, 94:22, 117:7, 125:16, 132:6 overhang 138:20, 153:1, 153:8 overhangs 154:1, 154:7 overlap 133:1 overview 19:5, 20:10, 20:16, 90:6 overwhelming 116:13 own 30:3 owner 1:10, 3:10, 4:2, 7:7, 10:4, 11:1, 49:16 owner's 5:18 P packaged 85:20 page 5:2, 5:10, 13:12, 38:13, 38:19, 40:15, 42:1, 43:12, 49:4, 50:16, 59:18, 59:19, 59:20, 60:2, 68:1, 72:19, 73:9, 79:7, 79:8, 80:13, 80:14, 80:22, 81:6, 81:7, 81:18, 93:7, 93:10, 93:18,	94:9, 94:11, 95:10, 96:20, 97:1, 100:2, 103:16, 105:3, 105:9, 116:11, 118:21, 135:5, 135:14, 141:13 pages 1:21, 105:13, 139:4 pair 122:20 pairs 99:1, 101:6 panel 83:21, 84:1 paper 11:16, 134:7, 136:12, 136:17, 136:20, 137:3 paragraphs 20:9, 20:14, 20:19, 21:2, 21:5, 24:15, 24:17, 26:17, 27:8, 27:13, 27:20, 39:17, 61:12, 104:9 parallel 83:16 parcel 129:3 parkway 3:5 parse 1:4, 7:10 parse's 11:4, 11:16 part 10:1, 15:22, 16:12, 17:7, 17:8, 60:11, 61:15, 62:1, 62:18, 62:22, 78:7, 81:7, 97:9, 98:6, 102:11, 102:12, 105:4, 112:20,	114:4, 114:6, 115:6, 118:13, 125:9, 126:15, 129:3, 129:5, 129:21, 130:14, 144:15, 145:6, 145:18, 148:4, 152:7, 155:8 partes 5:13 particular 16:2, 51:14, 52:11, 53:8, 57:22, 58:5, 62:21, 69:10, 100:5, 100:12, 101:17, 127:20, 133:12, 138:10, 143:21 particularly 78:19 particulars 101:7 parties 159:20 parts 16:6, 27:5, 91:17, 118:4 pass 146:1 past 70:18 patent 1:1, 1:2, 1:10, 1:13, 3:10, 4:2, 5:17, 7:7, 10:4, 11:1, 12:17, 19:22, 20:7, 20:11, 21:6, 22:2, 22:14, 23:15, 24:8, 27:4, 27:10, 27:12, 27:16, 49:16, 58:8, 59:12, 64:1, 98:3, 103:11, 106:3, 115:2, 115:7, 120:21,
---	---	--	---

132:18, 132:19, 133:6, 139:18 pattern 123:15 pcr 122:14 people 120:20 percent 147:3 percentage 74:6, 74:8, 74:19, 75:1 performance 33:3 performing 156:13 perhaps 128:19 person 35:13, 45:22, 46:15, 52:15, 89:2, 142:18, 143:17 personal 159:13 personally 76:9 persons 34:5, 34:19, 36:2 pertinent 96:6, 96:8 petition 11:4, 11:5 petitioner 1:5, 3:2, 5:12, 7:10, 66:13 petitioner's 5:17 ph 1:16, 2:1, 5:3, 5:12, 5:16, 6:7, 7:12, 158:2 phrase 29:19, 45:3 pieces 77:19	place 23:2, 60:15, 91:8, 105:7, 139:21, 150:5, 159:16 places 25:7, 38:11 plain 95:1 plainly 111:3 platform 98:22, 99:4 platforms 98:7, 98:15, 98:16, 99:21, 100:3 please 7:4, 13:14, 13:22, 17:19, 19:10, 19:14, 20:4, 58:2, 59:16, 92:21, 102:15, 103:14, 103:21, 117:8, 118:15, 123:7, 137:13, 152:20 plos 136:20 plume 149:16 plural 110:9 plurality 15:3, 15:4, 15:14, 15:15, 20:22, 28:21, 29:8, 60:7, 60:8, 61:7, 61:8, 104:20, 104:21, 107:6, 107:13 point 21:4, 23:1, 23:19, 24:15, 26:12, 29:9, 36:11, 40:15, 41:10, 42:6,	54:20, 69:12, 71:21, 83:13, 88:11, 89:9, 91:14, 102:4, 110:17, 116:16, 117:3, 138:3, 138:19, 145:12 pointed 23:3, 129:20, 151:14 pointing 41:20, 62:11 poly(a 146:22 poly(t 68:12 poly-a 59:4, 62:6, 62:17, 63:2, 63:8, 64:17, 65:4, 65:6, 69:22, 70:2, 70:10, 71:6, 73:3, 73:11, 74:20, 75:18, 76:2, 146:6, 149:20, 150:2 poly-a-tailed 65:1, 65:13 polyadenylated 68:7, 68:13, 69:19, 74:2, 74:7, 74:9, 75:7, 75:13, 75:14, 146:22 polyadenylation 5:19, 6:2, 64:19, 65:8, 67:17, 68:14, 68:19, 70:7, 73:20, 74:14, 146:9, 147:5, 147:11, 147:12, 147:20, 148:22, 149:6 polynucleotide 15:5, 15:8, 15:15, 17:5,	17:6, 38:5, 38:17, 45:15, 45:16, 46:21, 48:20, 52:17, 104:21, 154:18 polynucleotides 15:4, 16:4, 19:2, 29:5, 29:12, 33:21, 38:8, 60:8, 60:9, 61:7, 61:8, 104:20, 139:12 pooled 107:12 popped 31:3 portion 15:13, 17:15, 89:12, 107:4, 108:13, 114:5, 114:8, 141:18, 142:2, 143:13 portions 16:18, 46:11, 101:15, 109:6, 132:14 posa 36:22, 39:7, 41:1, 42:11, 45:6, 45:10, 45:11, 45:18, 45:20, 46:19, 47:3, 49:9, 52:7, 53:9, 53:12, 55:10, 57:21, 85:9, 91:2, 92:4, 92:13, 92:14, 95:5, 116:15, 131:16, 140:15, 141:4, 141:15, 141:21, 142:4, 142:10, 143:4, 143:10, 144:8, 145:13, 155:20 possibilities 46:15, 47:6,
--	--	---	---

Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

184

47:22, 49:15, 54:18 possibility 47:3 possible 19:9, 30:1, 35:5, 35:7, 50:5, 57:13, 70:10, 108:21, 112:21, 113:16, 114:3, 122:6, 128:12, 129:13, 144:12, 151:16, 155:9 post-transcripti- onal 149:7, 149:11 posters 121:6 potentially 101:13, 128:19 practice 30:14, 33:7, 35:6, 35:7, 49:10, 55:6, 55:7, 92:18 preclude 48:13, 138:19 predicated 115:19 prep 33:9, 100:22, 102:11, 102:12 preparation 100:22, 102:7, 102:18 preparing 21:1, 106:12, 111:13 present 4:10, 117:22, 120:12 presented 90:3, 90:11 pretty 94:22, 95:1 previous 32:22, 159:6	previously 25:16 primary 147:7 prime 73:12, 112:3, 123:11, 146:20, 147:6, 147:8, 147:14 primer 62:7, 63:5, 63:13, 79:19 primers 34:15, 68:12, 77:16, 131:4 priming 32:5, 88:2, 88:18, 89:15, 122:13, 122:21 prior 73:16, 104:2, 104:19, 119:21, 138:5, 139:10, 140:18, 140:20, 144:15, 145:1 probably 11:9, 29:2, 59:8, 69:7, 97:12 problem 37:19, 140:6, 144:10 procedure 102:12 procedures 101:1 proceeding 8:13, 58:11 proceedings 36:9, 159:14 process 63:1, 63:10, 85:21, 90:6, 90:8, 91:6, 96:16, 112:21, 132:6, 147:13, 149:14, 149:17, 152:22	processed 112:9 processing 70:8, 111:20, 112:1, 112:14, 112:20, 147:8 produce 98:7 produced 107:10, 109:18 products 121:8, 147:10 profile 148:4 prokaryotes 5:20, 6:3, 64:14, 74:14, 146:6, 146:9, 147:12, 147:21, 148:22, 150:6 prokaryotic 64:4, 64:13, 64:20, 65:9, 67:18, 68:14, 68:20, 71:4, 73:21, 146:21, 147:1, 148:9, 149:8 prominent 117:1, 134:15 properly 150:9 proposed 138:3, 144:10 protocol 102:3, 116:16, 144:13 protocols 115:21, 130:19 provide 22:6, 22:9, 23:17, 25:17, 25:19, 28:20, 29:7, 33:3, 41:9, 42:18, 50:16, 52:2, 54:13, 54:14, 55:9, 77:2,	91:15, 100:3, 107:7, 131:3, 145:12 provided 22:18, 57:9, 57:17 provides 19:5, 32:9, 38:20, 39:6, 39:21, 40:16, 41:11, 43:13, 49:4, 50:17, 51:3, 130:18, 132:4, 132:15 providing 19:6, 51:20, 60:16, 71:17, 83:4, 85:5, 139:11 provisional 132:11, 133:10 publication 72:10, 72:14 publications 72:17, 108:22, 121:6 pull 103:10, 103:13 pulldown 131:3 purpose 17:1, 33:22, 34:6, 34:19, 35:14, 35:17, 35:19, 35:20, 36:1, 42:4, 44:20, 53:6, 55:10, 110:13, 122:19, 123:5 purposes 91:14, 150:9 pursuant 2:2 put 7:21, 10:20, 12:1, 21:13, 102:4, 112:12, 114:12, 121:5
---	--	---	---

Q	105:16, 114:9, 114:11	136:12, 138:17	reduce 140:17, 144:9
quackenbush 6:7, 9:16, 10:13, 10:20, 115:4, 116:3, 117:3, 137:16, 145:10	R	reads 14:7, 98:7, 99:16	reduced 159:12
quackenbush's 9:4, 9:7	race 149:16	ready 14:1	reducing 51:10
qualitative 74:13	random 30:18, 37:20, 38:14, 44:21, 54:16, 56:22, 102:19	really 32:8, 39:4, 64:12, 69:13, 89:12, 89:21, 101:7, 144:14, 156:11	redwood 3:5, 3:6
qualitatively 128:6	randomer 41:1, 42:6	reason 69:1, 140:5, 140:15, 140:16	refer 14:22, 18:1, 41:16, 58:7, 97:17, 104:4, 114:1, 124:1, 125:4, 132:1
quantitative 15:19, 17:14	randomers 53:10	recall 64:9, 70:17, 71:13, 79:3, 93:15, 103:8, 103:10, 106:15, 136:12, 143:10, 146:4, 150:12, 151:9, 152:18, 153:8, 153:21, 156:22, 157:1	reference 36:13, 41:19, 44:7, 52:4, 55:7, 138:5, 145:2, 150:15, 150:18, 150:20, 153:22
question 24:18, 27:6, 47:1, 48:3, 59:21, 69:6, 69:19, 76:22, 90:10, 94:21, 105:18	randomly 30:6	recess 66:3, 97:15, 133:18, 145:22, 157:4	referenced 5:10, 8:15, 9:10, 9:20, 58:21, 66:17, 72:6, 93:2, 133:20, 146:15, 148:19
questions 56:3, 146:5, 151:5, 152:16, 152:18, 155:22, 156:1, 157:5	range 42:18, 45:19, 47:6, 47:18, 49:7, 50:4, 52:7, 53:10, 55:6, 55:15, 56:20, 57:5, 70:8, 96:10, 113:20, 155:9	recognition 127:11, 135:8, 135:9, 136:2, 136:3	references 21:21, 139:11, 141:8
quick 157:3	ranges 49:21	recognize 134:6	referred 58:15, 80:14, 112:15, 120:11, 122:4
quite 64:21	ranging 98:18, 147:1	recognizes 135:2	referring 9:8, 43:21, 50:9, 107:21, 110:10, 125:3, 153:14
quote 18:18, 19:18, 36:19, 36:20, 38:17, 40:2, 40:11, 40:12, 43:7, 50:10, 50:15, 105:10, 105:13, 105:17, 105:20, 106:1, 106:11, 108:2, 111:8, 112:2, 112:3, 112:4, 114:9, 144:17	rather 100:17	recollection 136:13	refers 20:14, 20:19, 92:3, 95:16, 107:1, 107:2, 107:17, 124:7, 149:13, 150:19
quoted 114:6	reaction 32:6, 101:22	record 7:5, 66:1, 67:5, 97:14, 133:16, 157:9, 157:11, 159:13	reflection 140:14
quotes 20:8, 40:3,	read 11:4, 11:8, 11:14, 11:16, 11:20, 27:22, 54:17, 67:1, 67:12, 71:20, 98:17, 98:22, 99:5, 100:7, 101:15, 131:16, 136:16, 158:3	red 62:6, 62:7	
	read-on 7:2	redesign 128:14	
	reading 47:5, 135:12,		

refresh 136:13 region 138:6, 138:12, 154:16 regions 16:8, 147:9, 147:10 reich 4:3, 7:7 reich@groombridg- ewu 4:8 reiterate 32:22 relate 19:21, 89:22, 133:6 related 127:16 relates 13:4 relative 24:17, 159:18, 159:19 relatively 74:18, 98:17, 144:13, 147:13 release 29:10, 29:11, 29:12, 31:22, 126:11 released 29:15, 29:20, 30:8, 30:16, 30:18, 31:4, 31:6, 31:13, 32:15, 32:17 releases 29:7 releasing 28:19, 152:6 relevant 27:21, 46:13, 60:16, 78:9, 89:12, 89:21, 92:5, 130:12 relied 32:1	rely 68:12, 92:14, 131:2, 144:17 relying 45:11, 47:21, 49:15, 62:17 remember 11:9, 11:13, 11:21, 29:22, 58:22, 61:1, 70:19, 90:16, 92:1, 94:7, 103:5, 103:11, 106:17, 116:6, 116:8, 121:12, 156:8, 156:9 remote 1:16 remotely 2:2, 159:16 render 46:6, 46:8, 53:4, 156:14 rendered 70:16, 73:18, 75:19, 136:10 repair 96:21, 97:6 repeatedly 37:15, 40:9, 50:12, 92:3 rephrase 74:22 reply 5:17, 8:12, 8:22, 10:7, 10:16, 10:21, 11:16, 11:18, 11:19, 12:10, 12:13, 12:15, 13:6, 14:16, 17:18, 17:22, 18:3, 18:11, 19:11, 20:8, 23:20, 36:16, 37:6, 58:3, 98:10, 103:20, 113:18, 114:14,	115:11, 125:12, 140:4, 156:14 report 9:4, 9:7, 10:4, 13:15 reported 1:22, 159:11 reporter 2:4, 7:3, 79:14, 157:8, 159:4, 160:10 represent 7:5 representation 77:15 representative 87:11, 90:7, 145:15 represented 80:8 reputable 66:8, 72:13, 72:15, 72:17 require 32:6, 78:8, 116:18, 132:6, 140:7, 147:15 required 17:9, 17:15, 23:6, 31:9, 77:9, 85:4, 88:20, 116:1, 131:5, 145:17, 154:7 requirement 30:12, 102:13, 140:13 requirements 25:18, 138:22 requires 15:3, 89:11, 107:20, 138:6, 138:9, 138:11, 138:16 research 6:18 residues 147:2, 148:7	resources 120:21 respect 140:4 responding 9:16, 10:21 response 5:18, 9:4, 10:1, 32:22 restricted 55:12, 71:3 restriction 6:10, 118:11, 119:3, 119:12, 119:18, 120:5, 120:9, 121:19, 122:7, 122:8, 123:18, 123:20, 124:3, 124:11, 124:22, 125:21, 126:2, 126:10, 127:14, 129:3, 129:10, 134:16, 134:20, 135:1, 136:15, 137:1, 137:6, 150:17, 150:21, 151:9, 151:15, 151:16, 152:8 restrictions 116:14, 120:22 restrictive 71:20 reverse 63:12, 73:13 review 5:13, 90:15 revised 140:3 ribosomal 6:14 ring 67:13, 76:11 rings 121:11 rnr 1:22, 2:3, 160:9
---	--	--	---

rna 6:2, 6:14, 88:1, 108:14, 146:5, 147:20, 148:21, 149:8, 149:15, 149:17, 149:18 rnas 31:12, 33:6, 34:17, 65:7, 70:10, 74:2 roche 98:22 routine 49:10, 139:20, 141:16, 141:22, 143:6, 143:11, 144:6, 145:14 row 68:6, 68:10 rrna 73:5 rule 75:3, 75:6, 75:8 rules 11:3, 23:5, 23:13, 25:6, 27:2 run 101:4	12:3, 13:5, 13:7, 13:8, 13:11, 19:21, 21:8, 21:11, 21:12, 21:15, 21:21, 21:22, 22:3, 22:7, 22:11, 22:15, 22:19, 23:7, 23:9, 23:15, 23:18, 23:21, 24:9, 24:12, 24:22, 25:8, 25:12, 25:20, 26:8, 36:12, 45:17, 46:22, 48:20, 56:3, 60:21, 61:2, 61:15, 64:21, 73:9, 81:15, 82:6, 83:9, 83:13, 84:1, 84:5, 92:9, 96:19, 110:16, 128:4, 135:5, 141:5, 158:4 sample 17:5, 29:2, 29:10, 31:6, 32:18, 33:9, 33:21, 37:2, 37:13, 38:4, 38:5, 41:22, 44:13, 48:21, 60:8, 61:8, 71:17, 99:1, 100:22 samples 6:14, 20:17, 28:21, 29:8, 73:2, 100:17 say 11:12, 12:21, 13:9, 16:2, 16:4, 17:21, 18:15, 23:2, 23:20, 24:7, 28:1, 36:21, 37:10, 38:6, 40:6, 45:18, 46:16, 46:19, 49:5, 53:1, 57:18, 61:18, 62:4, 63:3, 63:10, 63:17, 67:11, 69:3, 69:15, 74:4, 74:16, 75:5, 75:11, 75:13, 75:15, 76:1, 76:14, 77:1, 77:22, 78:16, 82:8, 82:13, 83:7, 83:15, 84:18, 89:14, 91:16, 98:14, 99:10, 99:21, 101:6, 102:10, 102:13, 104:2, 107:9, 108:20, 110:13, 111:19, 113:1, 117:2, 117:11, 117:16, 118:9, 118:19, 119:19, 119:20, 120:4, 125:15, 125:20, 126:1, 126:2, 126:7, 126:20, 127:6, 127:8, 130:2, 137:15, 138:9, 139:7, 139:10, 141:9, 141:15, 142:17, 144:5, 144:14, 144:22, 152:2, 156:11 saying 23:1, 24:11, 25:11, 26:2, 30:22, 48:10, 48:11, 56:18, 65:11, 74:10, 75:22, 85:16, 86:1, 87:2, 87:6, 88:7, 94:5, 109:11, 115:16, 122:5, 126:21, 127:10, 127:14, 128:3, 128:4, 128:13, 129:15, 136:18, 142:18, 143:10, 144:1, 150:7 says 15:14, 19:4, 21:15, 21:19, 38:3, 45:9, 51:6, 68:7, 72:21, 72:22, 73:10, 82:2, 84:8, 84:11, 84:14, 94:15, 96:21, 97:6, 100:3, 106:8, 106:11, 107:2, 112:9, 135:1, 135:6, 135:22, 137:20, 138:2, 146:20 scheme 30:5 schemes 48:15 scientific 22:9, 22:19, 23:17, 25:7, 26:18 scope 10:3, 31:21, 33:13, 51:8, 52:9, 53:11, 96:10, 142:15, 148:12, 154:13, 155:3, 155:15 scratch 83:15 scrna-seq 68:12 scroll 46:4 seal 160:2 search 27:6, 122:6
s safe 75:11 said 19:13, 25:16, 32:19, 32:20, 35:2, 47:19, 53:1, 54:19, 55:14, 59:10, 71:5, 74:18, 80:7, 90:13, 90:14, 98:5, 102:9, 103:5, 113:12, 126:4, 135:18, 159:15 same 11:18, 11:22,	

Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

188

second 13:12, 13:18, 58:18, 59:7, 60:1, 72:22, 73:9, 93:5, 95:14, 105:17, 105:20, 106:1, 118:21, 133:17, 135:19, 144:4, 144:9, 144:20 second-to-last 46:18 section 14:20, 51:15, 51:17, 52:2, 53:15, 60:6, 86:5, 94:22, 115:2 see 8:8, 8:17, 14:14, 17:13, 18:13, 18:14, 18:19, 19:16, 22:1, 37:4, 41:15, 43:7, 58:7, 58:10, 60:6, 61:13, 68:4, 68:7, 68:16, 68:17, 73:6, 73:14, 73:15, 80:14, 81:1, 81:19, 82:1, 83:15, 86:2, 86:4, 93:10, 93:13, 93:20, 94:12, 94:14, 95:12, 95:14, 97:5, 99:2, 99:19, 100:2, 102:18, 103:17, 103:19, 104:14, 105:10, 107:1, 111:12, 118:19, 119:4, 122:1, 123:13, 124:20, 134:9, 134:22, 135:4, 135:11, 135:20,	136:7, 136:8, 137:22, 146:20, 147:17, 147:18, 149:9 seem 145:10 seemed 145:11 seen 156:6, 156:10 selection 30:6 sells 134:19 sense 33:16, 100:13, 108:11, 148:1 sentence 26:2, 42:8, 43:22, 44:5, 45:9, 46:18, 51:14, 68:11, 72:19, 72:22, 73:10, 109:10, 111:19, 112:15, 120:4, 127:16, 137:15, 143:15, 143:22, 149:9 sentences 43:15, 52:13 sequence 6:8, 15:18, 16:3, 16:5, 16:11, 16:16, 16:22, 17:4, 45:13, 59:2, 63:2, 63:5, 63:7, 88:2, 100:4, 100:19, 101:11, 121:18, 122:11, 122:19, 123:4, 124:10, 128:9, 135:6, 135:8, 135:10, 135:22, 136:2, 136:4, 138:7, 138:10, 152:17, 152:21, 153:14,	154:5, 154:6, 155:13 sequenced 15:8, 16:1 sequencer 102:5, 112:12 sequences 15:5, 15:15, 20:18, 38:18, 42:7, 96:2, 104:22, 113:13, 122:1, 138:4, 147:15, 151:14, 153:21, 155:1, 155:2, 155:7, 155:9 sequencing 6:13, 15:3, 15:14, 19:2, 19:9, 21:9, 73:1, 97:18, 98:2, 98:15, 98:16, 99:4, 99:15, 99:17, 101:4, 101:22, 103:9, 103:17, 104:4, 104:19, 106:7, 111:21, 112:5, 114:4, 142:6 series 17:8, 33:1 serve 91:1, 91:13 serves 150:9 set 28:7, 38:22, 88:9, 117:19, 138:4, 142:4, 142:10, 160:1 sets 110:5 several 36:9 shape 52:19 shaped 12:13	shared 28:4 sheet 158:7 shores 3:5, 3:6 short 98:3, 98:17, 99:16, 99:17, 100:3, 101:5 short-fragment 112:3 short-read 98:7, 98:15 shorter 101:3, 147:1 shorthand 2:3, 159:4, 160:10 shotgun 103:9, 103:17 should 12:21, 28:1, 67:7, 72:1, 72:2, 72:15, 105:8, 113:1 show 14:12, 20:5, 118:22, 119:22, 121:6 showing 40:3, 133:9 shown 62:5, 81:11, 82:2, 82:9, 82:13, 83:19, 84:12, 94:15 side 80:16, 80:17 signature 158:10 signature-mig2k 160:7 signed 158:7 similarly 99:10 simply 14:12, 18:21,
---	--	--	--

86:17, 153:13, 155:12 since 145:9 single 20:13, 20:17, 20:22, 21:9, 28:2, 28:20, 29:7, 29:11, 29:13, 29:15, 29:21, 30:8, 31:7, 32:15, 45:14, 45:17, 46:22, 48:20, 48:21, 107:5, 107:6, 107:12, 107:13, 110:11, 138:6, 138:11, 138:16, 138:20, 139:2, 153:1 single-cell 6:16 site 88:2, 89:15, 118:12, 119:3, 119:13, 119:18, 120:5, 120:9, 120:10, 120:12, 120:15, 122:9, 122:13, 122:21, 123:18, 124:3, 124:7, 124:12, 124:14, 124:22, 125:7, 125:10, 125:14, 125:21, 126:2, 126:10, 126:19, 127:1, 127:3, 127:14, 127:20, 128:1, 128:18, 129:3, 129:10, 129:19, 129:20, 130:1, 130:2, 130:4, 130:6, 130:16, 131:21, 136:15, 150:22, 151:9, 151:15, 152:5, 152:8	sites 88:18, 120:22, 121:7, 121:19, 122:2, 122:4, 122:7, 123:1, 125:17, 127:11, 130:21, 134:16, 137:1, 137:6, 137:7, 147:5, 147:7, 147:9, 147:11 sitting 30:1, 34:18, 129:9 size 37:2, 37:13, 41:22, 44:13, 101:21 skepticism 69:5 skill 34:5, 34:19, 35:14, 36:2, 45:22, 46:15, 52:16, 89:2, 120:20, 142:10, 142:18, 143:17, 148:6, 153:11, 154:4, 154:21, 155:11 skip 7:18, 114:17 small 74:19, 75:1 solid-phase 96:17 solve 37:18, 44:22 some 9:4, 13:3, 15:20, 17:4, 29:4, 29:9, 31:9, 33:16, 48:7, 59:6, 59:10, 60:22, 64:12, 64:19, 65:13, 70:1, 77:8, 77:15,	87:22, 99:7, 102:4, 107:4, 110:17, 145:11, 146:5, 148:1, 148:3, 152:16, 154:16 somebody 8:9 somehow 78:1, 88:7 someone 148:5, 153:11, 153:13, 154:3, 154:21, 155:11, 155:13 something 48:14, 67:7, 70:17, 121:9, 129:4, 132:4 sometimes 17:21 somewhere 85:14 sorry 8:17, 12:21, 24:4, 40:19, 40:20, 47:1, 47:16, 52:20, 55:19, 56:11, 58:9, 59:7, 59:9, 59:20, 81:4, 83:15, 87:15, 95:9, 96:20, 97:1, 97:2, 99:5, 99:11, 99:20, 99:22, 103:16, 105:8, 107:1, 111:5, 113:10, 115:6, 115:8, 115:10, 117:12, 119:20, 122:17, 124:3, 127:8, 131:10, 132:18, 135:12, 135:14, 136:8, 138:15, 154:9, 154:10, 154:11	sort 13:2, 19:6, 20:10, 30:5, 30:6, 30:22, 32:10, 100:22, 104:4, 110:15, 129:1, 129:14, 149:14 sorts 77:2 sounds 85:22, 115:16 space 62:12 speak 21:2 species 75:2, 147:4, 148:9 specific 10:11, 12:7, 15:13, 17:14, 30:12, 32:9, 39:5, 39:20, 48:5, 48:11, 48:12, 49:3, 52:8, 52:18, 54:22, 55:16, 60:16, 87:19, 89:22, 91:14, 116:19, 126:22, 127:1, 127:18, 128:9, 128:13, 132:21, 141:8, 143:15, 144:18, 147:15, 154:6 specifically 12:14, 38:13, 41:16, 42:9, 43:12, 46:13, 57:20, 60:18, 69:18, 70:19, 70:20, 137:8, 156:9 specification 133:3, 133:5, 133:13 specificity 6:9, 143:2
--	--	---	--

specified 159:17 specify 15:13, 54:6, 54:21 spoken 12:11 stabilizes 153:4 stably 154:17 stamp 38:16, 43:4, 44:1, 50:2, 53:21, 54:16 stamps 44:18 stand 59:4 standard 45:21 start 10:15, 107:8, 127:13 started 56:12 starting 20:8, 99:14, 119:8, 123:11, 135:19, 137:21 starts 29:1, 29:3 state 19:16, 24:1, 24:21, 26:11, 27:2, 35:17, 45:1, 47:2, 51:12, 144:22, 151:6, 151:13, 159:5 stated 23:12, 144:22, 151:12, 153:6 statement 15:18, 17:13, 20:2, 21:14, 22:2, 22:14, 23:14, 25:9,	30:21, 32:10, 32:13, 35:20, 36:21, 43:2, 51:16, 52:15, 52:18, 54:4, 67:17, 68:19, 69:2, 69:11, 74:1, 82:2, 136:9, 142:14 statements 18:22, 73:17, 74:16, 75:10, 76:4 states 1:1, 149:6 stenographically 159:11 step 19:7, 52:12, 63:12, 86:20, 104:4, 106:7, 108:4, 108:15, 112:11, 112:21, 113:5, 114:4, 122:22, 137:17, 138:13, 138:17, 140:12 steps 17:8, 18:17, 18:18, 32:4, 33:2, 86:21, 92:19, 103:7, 104:5, 112:19, 139:20, 154:19 steve 3:16, 7:6 steven 3:11 still 33:7, 33:12, 61:15, 118:16, 141:14 stone 3:12, 4:4 stop 39:16 strand 59:3, 62:5,	62:9, 63:13, 135:9, 135:10, 136:3, 136:4 stranded 138:6, 138:11, 138:16, 138:20, 139:2, 153:2 strategy 37:21, 38:2, 40:22, 41:2, 42:4, 44:21, 44:22, 51:9 street 3:13 stretch 125:2 stretches 98:17, 100:4 strike 156:18 stripped 128:22 strong 66:9, 133:4 structure 94:15, 95:2, 95:22, 131:18 structures 86:10 subject 21:3, 156:5 subset 31:16, 32:12 subsets 34:17 substance 12:1, 88:12, 88:14, 89:16, 89:18 substantially 31:6, 32:18, 34:7, 34:21, 35:16, 36:5 sufficient 23:18 suggest 27:9 suggesting 49:14	suggestions 12:5 suggests 44:3, 53:2, 54:1, 130:15, 147:12 suitable 111:21, 112:4 suite 3:13, 4:5 summary 19:7 support 5:12, 5:16, 132:15, 133:10 supportive 132:12 suppose 10:2, 15:16 sure 7:6, 7:20, 11:3, 29:17, 54:11, 58:13, 67:11, 67:16, 67:20, 70:6, 71:8, 75:4, 90:15, 103:13, 106:17, 106:19, 107:9, 121:11, 152:22 surprise 33:14, 121:17, 124:2, 124:10, 126:3 surreply 11:2 swear 7:3 switching 122:12, 122:22 sworn 7:11, 7:14, 159:8 sydorick 4:11 synthesis 32:5, 59:3, 61:20, 62:8,
---	--	---	--

Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

191

63:13, 82:4, 82:15, 83:8	63:12, 65:6, 79:19	49:20, 54:19, 56:20, 57:13, 61:6, 77:4, 82:17, 82:21, 83:2, 85:2, 86:8, 86:13, 88:4, 88:11, 88:17, 89:10, 89:13, 89:16, 100:11, 106:6, 110:4, 110:20, 112:19, 113:4, 115:7, 116:12, 143:3	tend 98:7
T	tailor		tends 148:1
table	47:12		term 107:2, 107:21
68:3, 69:10	tails		terminology 108:20
tag	6:4, 76:2, 149:1		terms 12:12, 17:15, 42:5, 52:8, 94:21, 109:18, 140:19
15:22, 16:5, 16:9, 16:11, 16:12, 16:13, 16:17, 16:20, 16:22, 20:18, 44:17, 45:13, 56:22, 63:19, 82:10, 84:12, 89:13, 122:13, 122:21, 140:6, 140:15, 140:16, 144:4, 144:9, 153:5	take 58:2, 66:1, 71:14, 71:22, 103:14, 106:19, 112:12, 122:15, 123:6, 145:21, 146:19, 148:14, 149:5, 153:6, 157:3	talks 20:11, 20:15, 28:2, 34:14, 41:5, 41:17, 42:9, 43:16, 44:8, 51:4, 84:5, 92:12, 95:22, 107:22, 110:21, 112:18, 131:10, 132:14	testified 7:14, 36:8, 67:15, 102:6, 118:5, 129:2, 129:5, 137:1, 147:21, 156:20
tagged	taken 112:20, 159:15		testify 159:8
15:4, 15:7, 16:4, 19:2, 21:1, 38:6, 45:14, 45:16, 46:21, 48:19, 52:17, 60:7, 61:7, 61:19, 61:20, 62:18, 104:20, 154:18	taking 150:5		testifying 133:8
tagging	tales 6:5, 149:1	targeting 34:13	testimony 23:11, 37:6, 49:11, 98:1, 98:12, 108:5, 116:10, 126:17, 128:8, 150:12, 151:10, 158:4, 158:6, 159:14
19:1, 19:9, 21:9, 28:3, 38:6, 85:3, 142:6	talk 14:17, 16:19, 20:20, 21:7, 23:4, 25:17, 37:16, 38:15, 41:8, 41:15, 42:3, 42:16, 43:10, 46:14, 48:5, 50:15, 55:9, 55:17, 78:11, 82:7, 83:12, 118:2, 139:16, 141:1, 142:19, 143:3	teaches 18:16, 20:21, 40:4, 61:19	text 12:7, 21:4, 47:5, 68:10, 82:2, 91:9, 92:16, 133:13, 143:7
tags	talked 38:21, 39:13, 40:13, 49:1, 49:2, 49:3, 52:3, 53:19, 71:16, 79:18, 116:4, 123:22	tech 12:14	
16:8, 33:21, 38:7, 142:7	talking 11:21, 12:9, 24:4, 42:12, 43:14, 44:5, 44:16, 46:5,	technician 4:11, 7:2	
tail		techniques 139:19, 141:4, 143:5	
59:4, 62:6, 62:17, 63:8, 64:17, 65:4, 69:22, 70:2, 71:6, 73:3, 73:11, 74:20, 75:18, 79:20, 146:6, 149:20		technologies 98:2	
tailed		technology 99:15, 99:17	
62:7, 63:5,		tell 6:4, 149:1	
		telling 109:15	
		template 122:12, 122:22, 149:16, 150:1	
		templates 130:11	
			th 3:13
			thank 18:10, 56:14
			thanks 9:14, 118:17, 157:6, 157:7
			themselves 7:5, 47:10, 53:13, 133:14
			theoretical 137:6

theory 137:16 thereafter 159:12 therefore 23:7, 107:11 therein 9:5, 34:3 thereof 109:6 thing 48:13, 54:4, 128:20 things 8:3, 10:2, 10:12, 13:21, 47:18, 50:14, 85:7, 85:8, 85:9, 128:5, 144:7 think 15:12, 16:21, 19:4, 19:7, 21:7, 21:12, 22:18, 23:16, 23:18, 26:7, 28:13, 31:1, 31:8, 31:9, 31:20, 32:8, 32:20, 34:1, 34:9, 37:14, 46:3, 46:11, 49:7, 50:4, 52:22, 57:10, 58:14, 60:21, 64:9, 64:18, 64:20, 64:22, 65:6, 65:20, 69:7, 70:13, 70:17, 71:18, 71:19, 74:1, 74:18, 74:22, 75:5, 76:12, 89:7, 90:9, 91:16, 92:13, 94:5, 98:5, 98:11, 100:20, 102:2, 102:9,	102:11, 108:1, 108:7, 108:19, 109:6, 109:14, 109:17, 110:15, 110:17, 110:18, 112:10, 112:18, 117:4, 118:13, 120:13, 123:2, 123:22, 124:1, 124:6, 125:8, 125:9, 128:12, 129:18, 130:8, 130:19, 132:5, 133:22, 142:3, 143:21, 155:6, 156:16 third 99:14, 123:12 thought 90:13 three 27:7, 36:11, 117:11, 124:19, 137:21 through 6:14, 7:18, 13:2, 28:14, 48:22, 54:12, 119:15, 132:13, 136:16 throughout 38:12, 39:4, 77:1, 78:5, 92:3 thursday 1:17 thymines 59:2, 63:6 time 11:19, 11:22, 12:3, 73:17, 83:13, 95:5, 97:13, 98:2, 99:16, 118:2, 120:21, 149:4, 157:6, 159:16 times 7:18, 11:10, 27:7, 39:14	timing 102:3, 138:10, 140:1, 140:2, 140:10 today 23:11, 34:18, 129:9, 156:7 together 44:19, 80:15, 85:20, 107:4, 107:12 top 93:10, 93:21, 95:11, 100:2, 135:6, 135:9, 136:3 topic 21:12 totally 49:10 tracks 146:22 trademark 1:1 transcribed 65:4, 107:10, 107:22, 110:20, 149:15 transcript 150:2, 159:10 transcription 63:12, 73:13, 149:17, 158:5 transcriptome 107:5 transcripts 65:10, 67:19, 68:15, 68:21, 75:1, 75:7, 75:12, 75:14, 147:7 transitively 22:11 translated 13:10 translation 96:22, 97:7 treat 69:4	trial 1:2 true 20:2, 64:18, 65:20, 69:2, 69:11, 74:2, 74:4, 74:7, 81:15, 83:9, 84:1, 92:9, 100:20, 101:19, 101:20, 128:12, 158:4, 159:13 truth 159:8 try 18:7, 35:12, 66:14, 92:17 trying 30:13, 34:10, 35:11, 151:13, 152:2 tso 82:3, 82:9, 82:14, 82:17, 82:18, 82:21, 83:2, 83:7, 85:8, 85:11, 87:8, 88:3, 94:15, 95:2, 95:6, 117:17, 118:3, 119:1, 120:1, 143:20 tsos 83:5, 86:9, 86:11, 87:3, 88:5, 90:6, 90:22, 91:3, 92:4, 92:6, 116:2, 131:6 turn 59:16, 59:18, 61:11, 68:1, 93:7, 93:18, 137:12, 141:13 turning 80:22, 81:6, 81:18, 81:22, 94:8, 95:4,
---	--	---	---

95:9, 103:20, 105:2, 113:17 two 12:4, 20:12, 21:6, 21:16, 27:5, 27:7, 27:13, 27:20, 52:13, 57:4, 66:11, 85:8, 94:7, 105:15, 110:14, 117:11 type 6:9, 121:18, 135:1 types 84:16, 84:19 typewriting 159:12 typical 45:6, 94:15, 95:2, 95:22, 118:2, 118:3 typically 43:4, 43:17, 44:1, 44:9, 49:6, 73:3, 74:8, 98:18 U unclear 137:17 under 86:5, 142:3, 159:12 underneath 36:20 understand 19:18, 22:22, 29:17, 30:13, 31:18, 34:6, 34:19, 35:11, 35:14, 36:3, 42:11, 53:10, 55:10, 85:10, 92:5, 92:17, 153:12, 154:4, 154:22, 155:12 understanding 8:21, 9:3,	9:15, 9:22, 10:6, 10:14, 10:19, 23:4, 23:12, 25:5, 25:18, 27:21, 30:7, 54:11, 65:12, 74:21, 85:17, 95:7, 96:9, 125:5, 147:20, 150:4 understands 109:3 understood 61:4, 96:6, 108:18 undertook 19:18 unique 38:7, 38:8, 39:2 uniquely 38:6 uniqueness 38:9, 41:3 united 1:1 universe 19:8, 122:6, 137:5, 141:3 unless 26:12 unlike 73:1, 73:10 unquote 50:15, 144:17 unreasonable 27:9 untranslated 147:8 usage 30:3, 70:7 use 16:7, 16:9, 16:17, 35:4, 41:1, 42:12, 44:8, 44:21, 49:8, 49:9, 51:7, 51:9,	52:16, 53:7, 53:8, 53:12, 57:4, 76:15, 78:6, 78:12, 113:2, 116:15, 123:4, 128:21, 128:22, 130:20, 131:6, 131:21, 138:20, 144:11, 145:13, 145:16, 148:6, 152:9, 152:17, 153:14, 154:5, 155:7 uses 37:20, 86:9, 90:17, 95:21, 106:18, 149:16 using 16:20, 17:1, 39:8, 42:10, 48:18, 49:13, 54:6, 54:15, 60:3, 61:19, 82:9, 88:10, 100:19, 101:11, 108:8, 108:16, 108:19, 138:4, 142:7, 150:21, 155:13 usually 77:5 utilizes 20:18 V vague 91:11, 128:10 variability 43:19, 44:3, 44:5, 75:10 variable 39:1, 41:18, 42:21, 44:8, 44:18, 45:5, 47:11, 51:8, 54:14, 55:8 variable-length 43:16, 45:8,	49:1, 49:2, 51:9, 52:4 variety 149:19, 155:7 various 96:2 verb 108:15 versions 85:10, 85:12 versus 33:6 view 15:22, 68:18, 76:5, 78:3, 108:17, 109:2, 115:4 virtue 153:13, 155:12 W walk 13:1 walks 132:13 walter 3:3, 5:5, 7:9, 9:1, 12:19, 13:18, 13:21, 14:3, 15:10, 16:14, 17:11, 22:16, 24:2, 24:13, 25:1, 25:14, 26:4, 26:13, 28:10, 34:22, 49:17, 51:1, 53:16, 54:8, 55:2, 55:21, 56:9, 56:15, 67:4, 72:3, 76:18, 78:14, 82:19, 84:22, 86:6, 89:5, 90:20, 91:11, 100:9, 109:12, 112:6, 112:16, 120:16, 128:10, 134:3,
--	--	--	--

134:17, 142:21, 146:3, 146:16, 148:13, 148:20, 151:4, 152:1, 152:15, 153:20, 154:20, 155:10, 155:21, 157:8 walter@weil 3:8 want 7:20, 14:1, 14:19, 41:1, 69:5, 69:11, 101:14, 101:21 wanted 69:13, 103:7 warranting 117:6 washington 3:14 way 19:1, 19:3, 21:13, 30:9, 30:13, 31:10, 48:4, 58:13, 64:21, 65:2, 65:12, 65:18, 65:19, 67:11, 75:4, 76:5, 103:11, 108:8, 108:9, 108:16, 108:19, 110:16, 123:17, 124:17, 125:6, 126:20, 127:22, 129:8, 131:9, 136:13, 142:7 ways 31:14, 32:11, 52:18, 128:15, 140:21, 141:6, 144:3 we'll 7:18, 134:3 we're 24:4, 43:14, 44:5, 44:16, 47:9, 56:20,	57:14, 61:6, 81:2, 81:19, 82:21, 83:2, 85:2, 86:8, 86:12, 88:4, 88:11, 89:10, 115:12, 125:3, 129:1 we've 28:13, 54:12, 54:19 website 121:10, 121:18 weil 3:4, 7:9, 12:12 went 48:22, 101:1 weren't 67:16, 67:20, 117:2 whatever 15:20, 111:14 whereas 74:5, 130:1 wherein 20:9 whereof 160:1 whereupon 7:11, 8:14, 9:9, 9:19, 66:3, 66:16, 72:5, 93:1, 97:15, 133:18, 133:19, 145:22, 146:14, 148:18, 157:4, 157:10 whether 10:19, 67:12, 67:16, 68:18, 69:1, 69:21, 90:10, 103:8, 123:17, 124:10, 125:6, 128:1, 129:9, 132:11, 136:14, 146:5, 154:5 whole 16:22, 27:18,	42:6, 44:4, 44:20, 45:19, 92:15, 96:9, 108:12, 131:19, 159:8 wide 155:9 within 15:19, 19:6, 31:20, 33:3, 33:12, 38:5, 41:12, 42:18, 48:15, 52:9, 53:11, 62:20, 75:1, 75:10, 77:3, 77:4, 78:7, 79:22, 81:22, 86:11, 91:9, 96:2, 104:15, 117:22, 122:20, 129:18, 129:22, 133:13, 142:15, 147:9, 155:19, 159:4 without 14:2, 30:5, 128:22, 130:16, 131:7, 132:4 witness 5:2, 7:3, 7:11, 7:13, 8:16, 9:2, 9:11, 9:21, 15:11, 16:15, 17:12, 22:17, 24:3, 24:14, 25:3, 25:15, 26:6, 26:15, 28:12, 35:1, 49:18, 51:2, 53:18, 54:10, 55:4, 56:14, 56:17, 66:2, 66:18, 67:10, 72:7, 76:19, 78:15, 82:20, 85:1, 86:7, 89:6, 90:21, 91:12, 100:10,	109:13, 112:8, 112:17, 120:17, 128:11, 134:18, 143:1, 146:1, 151:20, 152:12, 153:18, 154:11, 154:14, 155:5, 155:17, 157:7, 159:7, 160:1 word 26:22, 27:6, 30:3, 30:9, 42:12, 43:22, 44:9, 49:13, 76:20, 109:8, 109:22, 110:7, 110:17, 110:18, 111:1 words 25:11, 26:12, 41:14, 43:10, 45:2, 62:13, 106:11, 107:16, 142:17 work 75:21, 92:18, 95:8, 120:7, 126:18, 128:2, 128:15, 155:1, 156:13 workflow 86:11 working 110:15 works 38:2, 40:22, 128:8 world 151:16 wouldn't 30:21, 31:15, 32:3, 56:2, 60:14, 64:11, 69:3, 69:8, 71:17, 74:15, 78:9, 94:6, 102:13, 108:20, 113:5, 113:7,
---	--	--	--

Transcript of Gregory Cooper, Ph.D.

Conducted on May 2, 2024

195

113:15, 126:18, 126:20, 138:19 written 9:3, 41:4, 41:13, 45:4, 49:22, 54:4, 57:5, 57:11, 57:15 wrong 35:21, 36:1, 58:21 wrote 69:9 wu 3:12, 4:4, 7:8 Y yeah 11:11, 18:5, 40:6, 55:5, 58:9, 67:22, 80:16, 80:17, 94:7, 99:12, 105:8, 105:17, 107:7, 110:6, 112:18, 115:11, 115:14, 119:15, 119:16, 122:18, 126:6, 135:15, 139:17 yep 7:22, 8:20 yohler 1:22, 2:3, 159:3, 160:9 york 4:6 yourself 75:17 .0024 4:7 .3000 3:7 .5832 3:15 0 0 135:2, 135:7,	136:1 00 1:18 00876 1:12 1 10 1:9 10,155,981 1:13 10017 4:6 1002 5:11, 9:18, 9:19, 12:21, 13:15, 14:6, 19:18, 20:5, 21:15, 21:17, 21:18, 22:13, 23:2, 24:1, 24:4, 24:17, 24:20, 25:13, 27:1, 27:14, 28:8, 37:10, 39:11, 42:13, 50:11, 58:17, 59:17, 69:16, 71:7, 71:14, 73:18, 75:19, 76:1, 76:14, 78:11, 78:21, 102:15, 104:12, 111:5, 141:21, 142:12 1002.071 60:4 1002.073 79:8 1002.075 80:14 1002.079 81:7 1002.099 105:3 1003 5:14, 36:13, 92:20, 93:1,	103:13, 105:21, 106:20, 123:6 1003.023 103:16 1003.024 93:7 1003.025 94:9 1003.026 95:10 1003.027 96:20, 97:3 1003.032 93:18 101 64:9 104 20:14, 24:16 1050 3:13 1059 5:15, 8:13, 8:14, 14:17, 14:22, 17:18, 18:1, 18:3, 18:12, 19:12, 20:8, 24:4, 24:7, 36:16, 58:3, 69:17, 71:7, 73:18, 75:20, 97:18, 98:11, 103:21, 113:17, 114:15, 114:19, 115:9, 115:10, 115:13, 117:9, 118:16, 118:17, 136:11, 137:12, 140:22, 156:15 1059.018 100:2 1059.086 141:14 1067 5:19, 146:8, 146:11, 146:14, 156:6, 156:13, 156:20	1068 6:2, 148:14, 148:18, 149:2, 150:5, 156:6, 156:13, 156:21 108 20:19, 24:16 11 62:5, 62:12, 62:16, 62:19, 63:4, 77:4, 79:9, 79:21, 80:15, 80:18, 81:8, 81:11, 81:16, 82:3, 82:14, 82:22, 83:12, 83:21, 84:12, 86:3, 92:9, 92:11, 103:4, 104:6, 116:14, 116:20, 117:13, 117:19, 120:11, 120:12, 122:4, 122:9, 123:21, 125:19, 126:3, 126:9, 126:14, 126:17, 126:22, 127:17, 127:19, 128:2, 128:4, 128:8, 128:9, 130:1, 137:9, 152:4, 152:5 113 137:11, 141:1 117 20:20, 24:16 119 139:5, 144:19 12 106:21, 109:9, 157:12 122 141:10, 141:15 126 19:11, 19:13, 19:14, 19:16 13 105:5, 105:21
---	--	--	---

PLANET DEPOS

888.433.3767 | WWW.PLANETDEPOS.COM

10x Genomics, Inc. Exhibit 2020
Parse Biosciences, Inc. v. 10x Genomics, Inc.

IPR2023-00876

Page 00195

Transcript of Gregory Cooper, Ph.D.
Conducted on May 2, 2024

196

133 6:10 139 61:12, 61:18, 78:21, 79:9 14 103:17 140 63:3 141 63:16 143 80:10, 80:19 146 5:5, 5:20 148 6:5, 81:1 15 100:2, 147:2, 148:7 153 81:6 154 81:15 156 5:6, 81:19 160 1:21 163 82:5, 82:8, 82:17, 83:10 164 82:1, 82:18, 83:8, 83:11, 83:19 165 84:7 166 84:1, 84:11 185 22:4 186 21:2, 24:16 187 21:19, 27:2, 27:14, 27:17, 28:2 19 105:6	192 42:16, 43:2, 46:2, 46:14, 47:2, 48:18, 52:14 194 21:2, 24:16 195 13:17, 14:6, 104:9, 113:20 198 104:11, 105:2, 105:19, 106:8, 111:4, 111:10, 113:21 199 104:9, 113:20 1997 146:10 1c 60:7, 60:19, 60:22, 61:16, 62:2, 63:22, 79:5, 86:22, 88:10, 89:4 1d 81:3, 81:8, 86:22, 88:10, 89:4 1e 81:20, 82:1, 83:3, 86:5, 86:17, 88:10, 89:4 1f 46:8, 46:13, 48:17, 49:12, 52:21 1g 14:13, 14:17, 15:1, 17:8, 104:15, 106:3, 114:12 2 2 135:2, 135:7, 136:1	20 47:8, 49:22, 52:4, 53:20, 55:18, 56:20, 57:5, 57:11, 97:13 20006 3:14 2006 149:4 2007002640 58:8 201 3:5 2013 6:6, 9:8, 9:9, 9:16 202.505 3:15 2023 1:12 2024 1:17, 160:3 206 38:15, 39:13, 39:15, 39:18, 41:5, 41:14, 41:20, 42:3, 42:9 21 105:4, 105:21 2101 6:8, 133:19, 134:1, 135:14 2102 6:11, 72:1, 72:5, 76:4 2103 6:16, 66:15, 66:16 22 103:14 23 93:11, 94:11 24 94:12 25 23:12, 26:16,	27:1, 27:13, 95:11, 105:5, 105:22 250 99:1 26 97:2, 99:21, 99:22 27 20:9, 24:15, 114:18, 115:8, 115:12 2728 68:3 28 105:6 29 18:11, 18:13, 18:15 2900 4:5 2nt 135:7, 136:1 3 3 94:16 31 93:20, 129:2 32 105:7 332.269 4:7 34 117:8 37 20:9, 24:15 3rd 160:3 4 42 126:1, 126:5, 126:6, 127:13 45 157:12 4531 2:4, 160:11
--	---	---	--

PLANET DEPOS

888.433.3767 | WWW.PLANETDEPOS.COM

10x Genomics, Inc. Exhibit 2020
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00876
Page 00196

Transcript of Gregory Cooper, Ph.D.

Conducted on May 2, 2024

197

454 98:22 4gs 88:3, 130:11 4n 39:3, 39:12, 39:19, 39:21, 39:22, 40:6, 40:12, 40:16, 43:11, 50:2, 50:9, 50:20 5 534770 1:20 54 14:22 565 4:5 6 6-to-8 54:16 60 147:2, 147:3, 148:7 63 99:9 65 103:22, 113:18 650.802 3:7 66 6:18, 59:18, 60:2, 118:14, 119:6, 119:16, 125:20 68 79:7 7 7-nucleotide 49:12 70 80:13, 114:14 72 6:15 74 81:6	763 38:19 764 38:19, 38:20, 44:15, 44:20, 49:4 8 80117 3:13 83 141:13 84 2:4, 160:11 85 36:16, 36:20 9 1:18 91 58:5 92 37:16, 38:3 93 5:14 94 105:13 94065 3:6 95 105:14 97 102:15 981 13:2, 19:22, 20:7, 20:10, 21:6, 22:2, 22:11, 22:14, 23:8, 23:15, 24:8, 24:11, 24:22, 25:11, 27:3, 27:10, 27:11, 27:16, 27:19, 27:20, 28:4, 28:15, 52:11, 59:12, 78:4, 83:6,	85:18, 89:18, 98:2, 115:2, 115:7, 120:21, 132:19, 133:6, 133:15, 139:18 99 20:14, 24:16	
--	--	---	--

PLANET DEPOS

888.433.3767 | WWW.PLANETDEPOS.COM

10x Genomics, Inc. Exhibit 2020
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00876
Page 00197