

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PARSE BIOSCIENCES, INC.
Petitioner

v.

10X GENOMICS, INC.
Patent Owner.

IPR2023-00876
Patent 10,155,981 B2

Record of Oral Hearing
Held: July 24, 2024

Before MICHAEL J. FITZPATRICK, SHERIDAN K. SNEDDEN, and
DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

APPEARANCES:

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The above-entitled matter came on for hearing on Wednesday, July 24, 2024, commencing at 1:00 p.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

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

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3 JUDGE FITZPATRICK: Good afternoon. This is IPR 2023-00876
4 Parse Biosciences, Inc. is Petitioner, 10X Genomics Inc. as Patent Owner. I
5 am Judge Fitzpatrick. With me virtually -- we're all virtually here it looks
6 like -- is Judge Snedden and Judge Zastrow Newman. Each side is going to
7 have a total of 60 minutes of argument time starting with Petitioner, and to
8 the extent either counselor or both wants to reserve rebuttal time, they
9 should make that known at the start. And this -- why don't we get an
10 introduction before both sides begin. Let's just get an introduction of
11 everybody who's on the call, starting with Petitioner's side, please.

12 MR. WALTER: Your Honor, this is Derek Walter of Weil, Gotshal
13 and Manges for Petitioner Parse Biosciences, and Alex Rosenberg of Parse
14 Biosciences is also on the call observing as well.

15 MR. BAUGHMAN: Your Honor, for Patent Owner 10X Steve
16 Baughman from Groombridge Wu. With me is my partner Megan
17 Raymond. And I believe we have some client representatives on the public
18 line.

19 JUDGE FITZPATRICK: Okay. Thank you. Mr. Walter, we'll begin
20 with you whenever you're ready. And we have the demonstratives. By the
21 way, we have the demonstratives of both sides. We also -- I'll acknowledge
22 that we saw that objections were filed. It's impractical to go through those
23 objections. That would eat up the entire hearing. We will take them under
24 advisement. The demonstratives though, in no way, shape, or form, are
25 considered argument or evidence of record. So I can't imagine any scenario
26 in which you could, for example, cite to the demonstrative in an appeal from

1 here or in a request for rehearing. My lights just went out. Let me get my
2 light back on. And so with that said, hopefully that reduces some of the
3 anxiety of what the other side is trying to put in through the demonstratives.
4 It's not really in. So an additional note, there are numerous Slides. Both
5 sides put in numerous Slides. I don't think it's realistic that you're going to
6 get through them. But I'll reserve final judgment on that as we begin. So
7 why don't you go ahead and proceed, Mr. Walter.

8 MR. WALTER: Thank you, Your Honor. I'd like to reserve 15
9 minutes for rebuttal. I'm going to begin sharing my screen. Your Honor, are
10 you able to see the presentation all right?

11 JUDGE FITZPATRICK: We are. And sometimes they'll be a delay
12 here because I try to mute myself when I'm not speaking.

13 MR. WALTER: Understood. All right. So I'd like to start my
14 presentation with a brief reminder on the claim language and a number of
15 pieces of evidence confirm that there is a serious invalidity problem with the
16 '981 patent. Here's Slide 2. I'm showing Claim 1. On Slide 3 I'm
17 identifying what are ostensibly the salient features. The claimed invention is
18 the use of two tags for the DNA in the single cell context. Now this claim,
19 this alleged inventive feature, is very much at odds with the specification
20 characterizes of the invention. Here is Slide 4. What the patent describes of
21 the invention is the reflex method. It's a method for rearranging a nucleic
22 acid molecule. You see that again on the summary of the invention on Slide
23 5, reflex, reflex, reflex, reflex, over and over. You try to count it up --

24 JUDGE FITZPATRICK: Counsel, can I just interrupt you. We are
25 well aware of this. But what I'm not fully aware of, what is the -- in your
26 opinion, what is legal ramification of this? How does that affect, for

1 example, the scope the claims or, you know, whether or not they are
2 obvious?

3 MR. WALTER: Yes. So it's a good question. It's a first clue that
4 there's an invalidity problem with these patents. The fact that the
5 specification describes something else other than tagging as being inventive
6 is a good indicator that tagging probably isn't inventive. And if you look
7 into the specification to get more into that, that's what you see. What you
8 see -- I'm showing Slide 8 -- tagging is something that was previously
9 described. It's not described as the invention. If you look at Slide 9, they
10 say the patent on the tagging was something that issued on July 2008, which
11 is more than a year before their priority date. Here it is again on Slide 10,
12 evidence on tagging previously was done. That's not new.

13 So that's your second clue, is that what the patent describes as the
14 invention is not the reflex method. What it describes is the invention -- what
15 it describes as the invention is the reflex method, not tagging. Tagging
16 characterizes the prior art. That's the second clue.

17 Now, let's find out -- let's look at the third clue. What does 10X think
18 about tagging? Well, they have this prior case against Becton Dickinson and
19 that case involved dual tagging in a single cell. Here's an example, it's on
20 Slide 11, this is Claim 13 that we discuss in our brief, and this is dual
21 tagging in a single cell context. It's the same stuff we're dealing with here
22 today. What did 10X say about this? Well, here we are on Slide 12 they
23 said it was well known and conventional. They said it was as old as the
24 scientific method. They said it was long-practiced. Here's another well-
25 known and conventional. Let's skip to Slide 19. Here's the claim chart from
26 their brief, one of the claims from that case. Two nucleic acid label tags.

1 Same thing we're dealing with here. How did they characterize it? Generic,
2 conventional, attaching techniques. So it's noteworthy that throughout this
3 case, 10X has pretty much ignored all of their prior statements. They've
4 never challenged the veracity of these statements. They've never said we're
5 taking it out of context. They've never said that what they said was wrong.
6 They just pretended it doesn't exist. That's your third clue that there's an
7 invalidity problem here.

8 Now, let's look at the file history. Let's go into our fourth clue. The
9 claims were allowed based on the prior art allegedly not disclosing a dual
10 tag. Here's the file history. The examiner said -- this is Slide 20 -- that a
11 dual tag was not in the prior art. In fact, that dual tag, that's the very thing
12 we just looked at, that's what 10X said was conventional in their previous
13 case. And, in fact, here it is on Slide 21, it is in the prior art. It's in the
14 McCloskey reference. So the examiner erred. That's your 4th clue that
15 there's a big problem here.

16 And now let's look quickly at the expert testimony in this case. I'm
17 showing Slide 22. This is their expert Dr. Quackenbush. He has no
18 opinions on objective indicia in this case. And I'm not going to go through
19 every one of these slides on this. Here's Slide 23. He says it again, no
20 objective indicia evidence. When you go through every single one, he
21 doesn't have any opinions. Here's Slides 24 through 25 through 30. No
22 commercial success. No unexpected results. No copying. No praise. No
23 long-felt need. That's notable. That isn't a situation where they're saying
24 hey, for a long time people had a hard time trying to do this. We asked him
25 about long-felt need, he says I'm not prepared to offer an opinion. This is a
26 supposed expert in the field. No teaching away. Nothing. But then you get

1 to Slide 31, and this one is very surprising. We asked him, what's inventive
2 about these claims? He says, I haven't done a thorough analysis of the
3 inventiveness at -- he says it's outside the scope of his report. He's their
4 expert on obviousness though. If he didn't do this kind of analysis, what did
5 he do? Let's look at Slide 32. Are you able to describe based on all your
6 work in this matter what you think is inventive about any of the claims.
7 Let's say someone wanted to know and asked you. I haven't performed that
8 analysis. It's outside the scope of my report. Now, the fact that their own
9 expert on obviousness had to dodge this question, which is a fair question
10 for an expert on obviousness about what's inventive, is one of the clearest
11 pieces of evidence I've seen that there's a serious problem with the validity
12 of these patents.

13 Now, I'm going to get right into their arguments. I'm going to start
14 with this claim term sequencing the --

15 JUDGE FITZPATRICK: Mr. Walter, a quick question. I've seen
16 there's been some stuff from district court that's been submitted here. Did
17 Mister -- or Dr. Quackenbush testify or submit a report opining on the scope
18 of the claims of the '981 patent in the related lawsuit in the federal district
19 court litigation?

20 MR. WALTER: He did. He did submit some evidence on that. And
21 as you might recall, we have submitted portions of that report that we
22 believe are inconsistent with his opinions in this case. And I'm going to be
23 presenting that very shortly. That's what I'm getting to right now.

24 JUDGE FITZPATRICK: Was that -- did he submit that prior to his --
25 to being cross-examined in this case? In this IPR?

26 MR. WALTER: No. It came afterwards.

1 JUDGE FITZPATRICK: Okay. Thank you.

2 MR. WALTER: Came afterwards. But what you'll see is
3 nonetheless, there's been a big change in opinion. So I'm going to start with
4 this claim term sequencing the tagged polynucleotides and how it ought to
5 be interpreted. I'm showing Slide 35. What we saw in the Patent Owner's
6 response was very surprising. They said the Linnarsson reference doesn't
7 satisfy the claims because it doesn't disclose sequencing the entirety of the
8 tagged polynucleotide. That was the argument. On Slide 36 I'm showing
9 their expert's declaration. Here's what he says, he says Dr. Cooper ignores
10 and doesn't address how Linnarsson sequencing of only a portion of each
11 tagged polynucleotide as opposed to the entirety of the tagged
12 polynucleotides could satisfy the limitation. He emphasized entirety. This
13 was their argument. This was their lead argument in their Patent Owner's
14 response. And what it was, was an attempt, kind of a stealth attempt, to try
15 to avoid the prior arts by construing the claims in a narrow way by alleging
16 that there's some sort of requirement for sequencing the entirety of the
17 tagged polynucleotides. Now, this interpretation is completely undermined
18 by the specification. This is Slide 37. The specification tells that you after
19 tagging, you actually break the polynucleotides down into bits before
20 sequencing so it can't possibly require that you sequence the entire thing,
21 and they've never challenged this. Now, even though Dr. Quackenbush had
22 opinions on this in his original declaration, on cross-examination he kind of
23 strangely said well, I never did the analysis. That's on Slide 38. We asked
24 him multiple times, do you have to sequence the entire polynucleotide? He
25 says well, I'm not prepared to render an opinion as to the scope of the
26 claims. That's Slide 39. On Slide 40, I haven't performed an analysis as to

1 the scope of the claims. Slide 41, I didn't perform a thorough analysis with
2 regard to claim construction. Slide 42, this one is very surprising, in the
3 context of preparing this report I haven't done a full analysis of the '981
4 patent and what's disclosed in the specification. So he didn't think about
5 what's inventive. He didn't fully analyze the patent or what's disclosed in the
6 specification. But whatever he did or didn't do in this proceedings, by the
7 time they got to the district court he was taking a very different position.
8 Here we are on Slide 43, here's Dr. Quackenbush's district court report that
9 we submitted. Here he states in black and white, the claims do not require
10 sequencing the entirety of the tagged polynucleotide. Now, my belief here is
11 that they realized this interpretation they were advancing was not just wrong
12 and inconsistent with the specification, but their narrowing spin might hurt
13 their infringement case. And so they're lead argument in their Patent
14 Owner's response, they've completely disavowed it. That was the first
15 argument they put in this attempt to kind of narrow the claims and it's gone.
16 It's gone. How do they explain this shift? The argument we're getting now -
17 - we started to see in their surreply as well -- all we're doing is we're
18 responding to what they included in their Petition, because their Petition was
19 relying on sequencing the entirety of the tagged polynucleotide, and here's
20 their reply. They cite --

21 JUDGE FITZPATRICK: Mr. Walter, I hate to interrupt you. Would
22 you mind going back one slide? I'm fully aware of what you're about to tell
23 us. I saw this and it jumped out at me reading the brief saying -- okay, then
24 what is -- I'm asking myself, I'm going to ask Patent Owner what is their
25 construction because it sounds like they want us to construe it in a way that's
26 advantageous to them without saying that construction. I get that. But this

1 position in district court that they took, the claims do not require sequencing
2 the entirety of the tagged polynucleotides. Has Petitioner taken a position
3 opposite of that in district court?

4 MR. WALTER: No, we haven't. What we've said is -- we've gone to
5 the district court and we've said hey, look. Look what they're doing in the
6 IPR. They're taking that narrowing claim construction. And if they take that
7 narrowing claim construction then we don't infringe. So that's the position
8 we've taken. To the extent the claims get construed this way, then we don't
9 infringe. We've never advanced that claim construction. We haven't asked
10 for it in the district court. And then when they saw that oh, there might be
11 an infringement problem, then they shifted gear completely. That's what I
12 believe happened.

13 JUDGE FITZPATRICK: Thank you. Sorry for interrupting.

14 MR. WALTER: Okay. So now to try to explain the shifting
15 positions in the IPR they have taken this -- they've adopted this story that,
16 hey, what's happening here is we're just responding to what they said in the
17 Petition. And this is in their surreply. They said hey, in the Petition, they
18 argued that you have to sequence the entire polynucleotide. And they cite
19 here our Petition at Slide -- our brief at 57 if you can see there. That's what
20 they cite. Let's look at what it says. Linnarsson teaches that after generating
21 the tagged polynucleotides sequencing is performed thereon. That's not
22 sequencing the entirety of the tagged polynucleotides. It doesn't say
23 anything of the sort. It just said you do sequencing on it. And let's look at
24 what they actually said on their Patent Owner's response before their
25 surreply when they're responding to page 57, here what they said. They said
26 that citation actually doesn't tell you what is sequenced. Let's go to Slide 47.

1 Let's see what Dr. Quackenbush said about this. We asked him, what do you
2 think, do you have to sequence the full thing or just part of it, and he says I
3 don't believe Dr. Cooper offered any opinions on this. So it's a little bit odd.
4 He said it twice. Here is Slide 48. He says I don't think Dr. Cooper offered
5 any opinions on this. So the whole argument is really odd. If it were really
6 true that the Petition and Dr. Cooper was presenting a combination that was
7 premised on sequencing the entirety of the tagged polynucleotides, their own
8 expert probably wouldn't come to a deposition saying Dr. Cooper didn't say
9 anything about that. And on top of that, they'd have something better to
10 show you. I'm going to show you their -- this is their Slide 25. This is
11 where they allegedly lay out the evidence for how we were requiring on
12 sequencing the full tagged polynucleotides. I don't see anything here.
13 There's a lot of words here, but there's no real clear statement to this effect.
14 And I'll just keep track of what they say during the argument, and I'll
15 respond in rebuttal.

16 Now, the next big argument I want to take on is the argument
17 regarding Figure 11, and this contention that Figure 11 is the only
18 embodiment in the specification. And I'm going to start with their Slide 7.
19 Here's what they say. Here's where they make this argument that Figure 11
20 is the only embodiment. They say Linnarsson's method requires biotin.
21 That's in the top there. And they say that biotin is critical -- you know, this
22 is where they make these arguments that Figure 11 is required. And the
23 evidence undermining this, frankly, is really overwhelming. Let's go to
24 Slide 86. Here's what the patent tells you about Figure 11 and the features of
25 Figure 11. The patent tells you that that the steps in Figure 11 are quote,
26 optionally used. It can't be that Figure 11 is the only embodiment and all

1 those features are required when Linnarsson tells you those are optional
2 features. That alone ought to be dispositive on this. And it's obvious and
3 clear it ought to be dispositive. But also what is just as obvious and clear is
4 when you actually look at the specific embodiments in Linnarsson and
5 compare them to one another. It's clear based on this that the approach of
6 Figure 11 is not the only embodiment. Let's go to Slide 84. Here's Figure
7 11, and it shows the biotin, and it shows the restriction enzyme cut sequence,
8 where it wants to use these things, it shows them. I've highlighted them in
9 yellow. Now, let's go to Figures 3 and 4 in the patent. Well, if you look at
10 Figure 3 there's no biotin. There's no restriction enzyme site. It's not called
11 out. It's just absent. You can see that in Slide 93 for Figure 4 as well. Now,
12 they've made some argument that there is actually a restriction enzyme site
13 for an enzyme. That's never once mentioned in the reference, which is really
14 dubious for reasons we've laid out in our motion to exclude. I'm showing
15 you their Slide 15 right now. You know, they -- what they've done is
16 they've gone and searched to see if there is some sort of restriction enzyme
17 sequence for some restriction enzyme that's never mentioned in the patent,
18 and they found one and they put a circle around it. That circle is something
19 they added that's not actually in Linnarsson. It doesn't identify that as a
20 restriction enzyme site it's undisputed that this for a restriction enzyme that's
21 never once mentioned in the patent. So this whole contention is really quite
22 dubious, I think. Here's their Slide 7 again. Actually, here's Slide -- here's
23 Figure 3 and 4 again. Even if you accept this assertion that there is some
24 sort of restriction enzyme sequence buried in there, there's no biotin. The
25 biotin is just missing here. It's just not there. Here's their Slide 7 again. As
26 I said, they say biotin is -- it requires biotin. Okay. They say it's critical.

1 Okay. If that were really true, you wouldn't have Figure 3 and 4 which don't
2 show a biotin and don't call out a restriction enzyme site, don't even
3 realistically have one that's used in the patent. Now, we're getting some sort
4 of argument that in Figures 3 and 4 there really is a biotin there. Well, let's
5 look at their expert, let's see what he says. We asked him, do you have any
6 understanding why there is no identification of biotin in Figures 3 and 4?
7 He didn't say oh, it's really there and if you look at the specification it tells
8 you it's there. He says I can't comment on why. He doesn't have an
9 explanation for this again. This is not the kind of answer you'd expect if
10 they were really intending for there to be a biotin there.

11 Now, the third point confirming that Figure 11 is not the only
12 approach, is that the CDS in Figure 11 doesn't include a cell tag. Okay.
13 Here's Figure 11 again, and if you look at the right-hand side you can see
14 here's the CDS. And the thing to note about the CDS is that it doesn't have
15 the X X X X X. Okay. It doesn't have the cell tag. Okay. Now, the CDS in
16 Figure 4 does. Now, it makes sense that the CDS in Figure 11 doesn't have a
17 cell tag because that's the end of the molecule that's not sequenced in that
18 particular example. But if you believe that Figure 3 and Figure 4 are the
19 same approach as in Figure 11, then you would have to believe that in Figure
20 4 Linnarsson included a cell tag only to completely ignore it. That makes no
21 sense at all. The whole point of the cell tag is to sequence it so you can
22 understand and determine which cell the DNA fragment came from. There's
23 never been any response on that point. In fact, we asked Dr. Quackenbush
24 about it. I'm showing that on Slide 88. We asked him, why would the CDS
25 be tagged if it was never -- if it was attached to a streptavidin and it never
26 cut for sequencing? The answer, I haven't done that analysis. There's a lot

1 of that from Dr. Quackenbush. There's a lot of non-answers what he gets
2 posed with a question that they, frankly, can't answer. There's no
3 explanation for this.

4 Now, another key piece of evidence, the 4th point, the embodiment in
5 Figure 11 can't possibly be the only embodiment because Linnarsson tells
6 you that you can include the cell tag on both the CDS and the TSO. That's
7 what it says. That's on Slide 87. But here's page 84. Here's Slide 84, again.
8 As I noted, there's no cell tag -- there's no cell tag on the CDS in this figure.
9 I'll say it again, Linnarsson tells you that their embodiments were in the
10 CDS as a cell tag, but there's no cell tag in the CDS in Figure 11. So the
11 approach of Figure 11 can't possibly be the only contemplated approach.
12 There has never been any response to this either.

13 Fifth, let's look at the claims of Linnarsson. Let's go to Claim 1. This
14 is Slide 121. If you look at Claim 1 of Linnarsson there's no biotin.

15 JUDGE FITZPATRICK: Mr. Walter, do you mind going back one
16 slide again? I had a question there. So going from A to B -- or let me put it
17 this way, and B is the first place in Figure 11 where you see the tag, right, at
18 least illustrated?

19 MR. WALTER: In Figure 11, Figure 11 is the first place. There is --
20 that is the first place it appears. There is no cell tag on the CDS. So this it's
21 not just the first place it's shown, this is the first place it appears in Figure
22 11.

23 JUDGE FITZPATRICK: Gotcha. And what introduced -- in your
24 opinion, what introduced that tag? Was it a TSO in this case?

25 MR. WALTER: Yes. This thing right here is a TSO. What happens
26 is --

1 JUDGE FITZPATRICK: Okay.

2 MR. WALTER: You have the extension and after the extension takes
3 place, the enzyme it adds a series of Cs. That's just the way the enzyme
4 behaves. That's just what it does. When it reaches the end of its
5 complementary piece of DNA it adds these Cs and then you can introduce
6 the TSO with the complementary Gs.

7 JUDGE FITZPATRICK: Okay. Thank you.

8 MR. WALTER: In Figure 11 that's the first place it appears. But in
9 other embodiments the CDS actually has a cell tag and it comes in earlier
10 and it doesn't have a biotin and you don't do this specific approach. The
11 other embodiments in Linnarsson, they have a lot in common with Figure
12 11, but they don't have every bell and whistle that it has.

13 All right. So let's look at the claims. Let's look at Claim 1. No
14 biotin, no restriction enzyme, no capture, no fragmentation. It's not in the
15 claims. Not in Claim 1, but it does appear in dependent Claim 27.
16 Dependent Claim 27 is the fragmentation approach. Here's their Slide 7
17 again. They say Linnarsson's method requires biotin. They say it's critical.
18 We asked Dr. Quackenbush about this. He said he reviewed Claim 1, but he
19 wasn't prepared to discuss it. He can't even state what it encompasses.
20 That's on Slide 22 and 23. On Slide 124 more of the same. He can't even
21 say whether it requires fragmentation. Slide 125, he can't even say whether
22 Claim 1 includes a biotin or not. We asked him about Claims 26 and 27. He
23 wouldn't say anything about that either. There's just more dodging the
24 evidence. I don't believe Dr. Quackenbush was a credible witness in this
25 case. That that doesn't mean we can't learn something from the very many
26 non-answers we received. I think the key point though is that if it were

1 really true that this method required biotin and that it was critical, you would
2 see it in the claims. You would see it all the descriptions. You don't see it in
3 all the descriptions. It's not critical. It's not required. It's not in the figures.
4 It's not in the claims.

5 Now, there's a little more on this. I want to show you Slide 111. We
6 asked Dr. Quackenbush a simple question. We said, you understand that
7 Figure 11 is just one embodiment? His answer if you look at the bottom, I
8 haven't done an analysis of all of the patent to the extent that I've looked at
9 all the possible embodiments. He doesn't even know if there's multiple
10 embodiments there. He says -- in his middle answer there he says Dr.
11 Cooper didn't discuss any other embodiments. That's not true. Let's go
12 through Slides 94 to 109. Dr. Cooper talks about Figure 3 over and over and
13 over again. He talks about Figure 4 over and over and over and over again.
14 It's in the Petition over and over and over. What about Dr. Quackenbush?
15 Sir, you're absolutely correct. I didn't cite to Figure 4. How come you
16 never addressed Figure 4? This is Slide 113. The previous one was Slide
17 112. So I don't explicitly call out Figure 4 in my analysis. So he ignored the
18 key pieces of evidence in this case that undermined their key theory. And,
19 you know, I would submit what he didn't do was he didn't take the prior art
20 for the whole of what it teaches.

21 Now, I want to spend a moment on one issue where they spend a lot
22 of time. I'm showing their Slide 84. Here they argue that our response to
23 their arguments on Figure 11 is new and improper reply. I'm showing their
24 Slide 81. The thing that you've got to look at here is is this raising new
25 issues? Is it introducing new prior art? Is it changing theories? None of
26 that is happening here. What's happening here is that in their Patent

1 Owner's response, they made an unsupported and frankly surprising
2 argument that the approach of Figure 11 was a sole approach in Linnarsson.
3 In our reply, we said two things. We said, no, that's incorrect. There's
4 overwhelming evidence that Figure 11 is not the sole approach of
5 Linnarsson, and Linnarsson tells you it's not. And we said that we didn't rely
6 solely on Linnarsson Figure 11. Here's the other stuff that we relied upon.
7 And we said that even if Figure 11 was the only embodiment, your position
8 is meritless because it's based on improper bodily incorporation. That's not
9 improper reply. That's fair reply that's responsive to meritless arguments.
10 And, frankly, I would submit that the extent to which we're getting all these
11 objections to evidence and all these arguments that the issues we're raising
12 are new is just -- it's not -- it's not real. It's a sign of weakness on the merits.

13 All right. I want to get to their next argument. I've taken this a little
14 bit out of order here. Before I move on, I want to know one thing. The
15 argument I just completed regarding the Figure 11 not being the only
16 embodiment, once you recognize that Figure 11 is not the only embodiment,
17 they put their heads in the sand and ignored the other approaches, they're in
18 Linnarsson and tried to make these, frankly, unreasonable arguments about
19 what Linnarsson discloses, once you realize that, that basically sweeps away
20 probably about 70 percent of their arguments in this case. All right.

21 Let me go to their next big argument, which is this idea of McCloskey
22 not having enough tags. Here's their argument. This is Slide 62. This is
23 Patent Owner's response. McCloskey doesn't have enough barcodes, they
24 say. And to be real clear, their argument is that they think you have to tag
25 every single molecule on a cell. You see that on their Slide 36 were they're
26 talking about 50,000 to 300,000 molecules. That's for a mammalian cell.

1 Now, this whole numerosity is argument without merit. There are several
2 reasons for that. First, the claims don't require that you sequence all the
3 molecules in a cell. I'm showing you Slide 63. The claims require that you
4 tag the sample polynucleotides. Now it's true that the sample comes from a
5 cell, okay. But it says sample, not all the polynucleotides in the cell, and
6 that's important. If you look at Slide 64, I'm showing you their district court
7 claim construction brief. Here's their argument. To argue that the sample
8 polynucleotides means every polynucleotide of the cell would rewrite the
9 claim and replace sample with all. Okay. So the claims don't require that
10 you have to tag all the polynucleotides in the cell, it's just the sample that
11 comes from the cell. The district court's claim construction opinion came
12 out after the briefing was in and the court agreed with 10X and we weren't
13 taking an opposite position. We all agreed on this during the district court
14 claim construction proceedings, you know, try to get ahead of a question you
15 might ask.

16 JUDGE FITZPATRICK: What -- yeah. What did you agree on? It
17 seems to me like the district court said sample doesn't mean all but -- so it's
18 less than all, but it's some unknown number. Is it two? Is two enough as
19 long as you have a plural?

20 MR. WALTER: Yeah. And I think the answer -- that ended up
21 being the dispute during the district court claim construction. They wanted
22 to broaden it. They wanted to -- here's the full history here. In a previous
23 case, they proposed a construction for a disputed claim term, and we agreed
24 to that claim construction. We thought it was an appropriate construction
25 that they had previously proposed and that had been previously adopted. In
26 this case, they suddenly wanted to change it. They wanted to change their

1 construction to something else. They wanted to change it to a requirement
2 that you have to tag the molecules of interest. That was their requirement,
3 and we were very concerned by that because it seemed vague. It seemed
4 like an attempt to try to broaden the claim in a way we couldn't understand,
5 and that's what we opposed. We said hey, don't do that, Your Honor, in the
6 district court. We said, take the old construction. Sample doesn't need to be
7 all. It can be less. And, you know, what you should be looking at is the
8 method by which you prepare the sample and you have your sample, that's
9 what you should be looking at. But it can't be this vague and loose of
10 interest language. That's where we ended up. Okay.

11 JUDGE FITZPATRICK: I saw that, but it didn't really -- that didn't
12 answer my question. Is there an answer to my question or no?

13 MR. WALTER: I think the answer to your question is that you have
14 to tag the molecules in your sample and the number of molecules that you
15 have in your sample is going to depend on your sample preparation method.
16 It's not going to be what you subjectively think is interesting, but it's going
17 to depend on your sample preparation method.

18 JUDGE FITZPATRICK: Can't you just -- can't you control that
19 ultimately by deciding what to call your sample? Deciding how to prepare
20 the sample?

21 MR. WALTER: And that I think is the issue, is that to some degree
22 you may be able to control that, but you can't always control that. And that,
23 I think, was part of the concern for us. Is that you could see them trying to
24 say that our method don't satisfy the prior art because this sample
25 preparation method is going to let in molecules that are not of interest.

1 JUDGE FITZPATRICK: So would you agree or disagree that two is
2 enough?

3 MR. WALTER: Two is enough.

4 JUDGE FITZPATRICK: Two polynucleotides is enough if they're
5 from the same cell?

6 MR. WALTER: Yeah.

7 JUDGE FITZPATRICK: The whole claim you could do with 4,
8 right, if you had two polynucleotides from one cell and two polynucleotides
9 from another cell? That would be enough to -- enough material to go
10 through the claim?

11 MR. WALTER: Yeah. Yeah. Yes.

12 JUDGE FITZPATRICK: Okay. Thank you.

13 MR. WALTER: So you know the whole argument about having to
14 tag all of them, it's just contrary to how the claims should be interpreted.
15 They're not really disputing this anymore in the district court.

16 So they've shifted to this argument that says oh, we're only
17 responding to the Petition which was premised on all the molecules on the
18 cell. I'm showing you their Slide 35. There's a lot of words on here, but
19 there is nothing in here where we've said that the Petition requires every
20 molecule. The closest one is this one here on the bottom, okay. But you
21 know what? That's not even the Petition in this case. That's a different case.
22 And if you look at what Dr. Cooper actually said, all he was saying was in
23 Linnarsson all the mRNA is released from the cell, so if you wanted to tag
24 every molecule you could, not that it's required. So I still don't know what
25 they're going to point to to support this argument that the Petition was

1 premised on tagging every single polynucleotide in a cell. I don't see in
2 here.

3 Now, the third point they argue is that the Petition was somehow
4 limited to using 7 nucleotides for the cell barcode. It wasn't. I'm showing
5 where this came from. They pulled this 7 nucleotide theory from Dr.
6 Cooper's report in this case. And here's what he said. He said right here, he
7 says a POSA could conceptually divide each of Linnarsson's cell tag
8 sequence into two portions. One portion you could use to track the cells and
9 the second you could use to differentiate polynucleotides. And then he gives
10 an example. He says for example, Linnarsson discloses that its cell tag can
11 be 4 to 20 nucleotides. McCloskey discloses that a -- typically comprises 6
12 to 8 and its barcode comprises 7. Therefore, a POSA could have
13 conceptually designated the first 6 to 8, and then used the next 7 to
14 distinguish the tagged polynucleotides. He doesn't say that seven is the only
15 thing you can do. That's an example. He says someone can conceptually
16 divide it up and he gives an example of how you could do it. It's misreading
17 of the Petition to say that this is the only thing Dr. Cooper was saying you
18 could do. Dr. Cooper gave an example on an approach based on McCloskey
19 and Linnarsson to illustrate the approach. To show obviousness Dr. Cooper
20 doesn't have to provide a road map for every possible experiment and every
21 possible sample type you're going to work with. In fact, if you look at the
22 disclosure of McCloskey it's general too. It tells you how many different
23 nucleotides you need to use if you want to distinguish a certain number of
24 polynucleotides. And then they say we use 7 right now. This is an example.
25 No one would read McCloskey is saying, hey, 7 is the key to life. And a
26 person of skill in the art is not an automaton. If they need to do more, they'd

1 increase the length of the number of the -- they'd increase the length of the
2 barcode.

3 Now, on Slide 78 we have Dr. Cooper explaining exactly this. He
4 also explains it in paragraph 85 of his report which is on Slide 79. And I
5 want to show you now Slide 80 where he says it again. And the point I want
6 to get to is that, you know, one of the things they've said in this case is
7 they've relied upon Dr. Cooper. They've relied upon his declaration from
8 another case. I'm showing that on Slide 80 right here. They relied upon his
9 declaration from another case to try to support this 7 nucleotide argument
10 and the idea that it wouldn't be obvious to use more than 7 polynucleotides.
11 He never said that. Here's what's shown on Slide 80. Here's his opinion
12 from paragraph 257, and he says a POSA with an easily designed tag
13 sequence is comprising 20 to 30 random nucleotide bases which would
14 allow for the creation of 4 to the 20 to 4 to the 30 unique barcodes
15 distinguishing among, and then there's two ungodly numbers. This is
16 argument that Dr. Cooper admitted that McCloskey is limited to 7 and
17 you're stuck with 7 and a person of ordinary skill in the art would be stuck
18 with this, that's not even what the testimony that they cite says at all. And,
19 in fact, Dr. Cooper says the exact opposite. And then what's interesting is
20 that we get the argument, oh, this is new this is new evidence that we're
21 being submitted. They submitted this. They submitted this declaration to
22 support their opinions. It can't be that they can submit Dr. Cooper's opinions
23 and then take what they like and then say the bad stuff is new and improper
24 opinion. In fact, his opinions that they rely upon say the exact opposite of
25 what they contend it says.

1 JUDGE FITZPATRICK: Mr. Walter, pause there. You got about, I
2 guess, nine minutes before you would get into rebuttal time. At some point
3 can you spend a little bit of time on Claim 5, the ligation claim?

4 MR. WALTER: Yeah. Let me do that right now.

5 JUDGE FITZPATRICK: Okay. And let me start with saying that,
6 you know, I saw in the cross-examination of Dr. Cooper where Patent
7 Owner tried to, you know, explore the idea of is Claim 5 -- are you taking
8 the modification of Linnarsson and McCloskey that meets the subject matter
9 Claim 1, and are you doing something additional to that to get to Claim 5?
10 Or are you starting over? I'm in the ballpark. I hope this rings a bell. I
11 remember --

12 MR. WALTER: Yeah.

13 JUDGE FITZPATRICK: -- Patent Owner counsel asking this and I
14 don't know that there was a definitive answer by your expert.

15 MR. WALTER: Yeah. So claim -- Ground 1 and Ground 2 are very
16 similar. In Ground 1 -- you know, obviously Ground 2 is a dependent claim
17 within scope of Ground 1. In Ground 1, you know, the example we've given
18 is that you could have a tag that's designed at the outset that has the two
19 barcodes, one region for the cell and one region for the molecular identifier.
20 The only way in which Ground 2 differs from Ground 1 is that you ligate the
21 tag onto -- you ligate the molecular barcode onto the cellular barcode. That's
22 the only way in which it's different, otherwise, it's the same thing. I think
23 Dr. Cooper said, yes, it builds on Ground 1. The only difference is is that
24 your ligating on the molecular barcode. That's the only difference. Does
25 that answer your question?

1 JUDGE FITZPATRICK: I don't know that it does. So once -- let's
2 say you design -- you're inspired by McCloskey starting with Linnarsson
3 and you now have this conceptually divided label -- I'll be generic. And
4 some of it is to designate the cell, and some of it is to uniquely identify the
5 polynucleotide. You already have that. And let's say you did it not using
6 ligation. How do you go from that to Claim 5? Or do you start over?

7 MR. WALTER: Well, you're not really starting over. I mean, the
8 concept of using two tags is still there. It's only how are you going to get to
9 the actual end-product with the two tags. Okay. That's the only thing. I
10 mean, maybe the best way to --

11 JUDGE FITZPATRICK: So are you going to ligate both tags? Or
12 are you going to have one tag, for example, be part of the TSO in Linnarsson
13 to ligate the second tag?

14 MR. WALTER: Yes, that's right. Because one of the things Dr.
15 Cooper said in his report is that you could ligate the molecular barcode to
16 the CDS or the TSO, okay. And so the CDS and the TSO of Linnarsson
17 already have the cell tag, and so you would ligate the barcode onto the CDS
18 or the TSO. And then you would have both tags. So you're not really
19 starting over. You're starting with Linnarsson and you're just introducing the
20 second tag albeit by ligation. Does that help?

21 JUDGE FITZPATRICK: It does. And so in your proposed
22 modification, it's -- one tag is already kind of built into the TSO and you're
23 going to ligate the second tag.

24 MR. WALTER: Yeah. And it could also be the CDS as well or both.

25 JUDGE FITZPATRICK: Okay. Yep. Yep. Fair enough.

1 MR. WALTER: Yeah. And Dr. Cooper states that in his report.
2 Okay. So I --

3 JUDGE FITZPATRICK: And the reason I ask is that because they
4 bring up -- they say that creates a whole bunch of complexity with zero
5 benefit. And I want to know what your -- you know, your response to that
6 is.

7 MR. WALTER: Yeah. So the response is, it doesn't create a whole
8 lot of complexity because ligation is conventional. That's the main thing.
9 This is the most straightforward thing you can do. It's admitted in the patent.
10 Dr. Quackenbush admitted it multiple times. Ligation was a conventional
11 technique. Ligation was a well-known method. Ligation was a method that
12 was well-known in the art before the priority date. I personally performed a
13 number of ligation. It can't create a whole bunch of complications because
14 of it's conventional.

15 Now, all of the complications that they rely upon, the arguments that
16 they rely upon are all stemming from this argument that -- I'll show you their
17 slide. This is the quickest way to get to this. All of their complications are
18 stemming from this argument that Figure 11 is the only embodiment. The
19 simplest example of their complication is that -- well, look here there's a
20 biotin here and because the biotin is here you can't ligate the oligonucleotide
21 tag to the CDS because the biotin is going to block you. But the problem is -
22 - the problem for them is that Figure 11 is not the only embodiment. There
23 are embodiments as in Figure 3 and Figure 4 that don't include the biotin.
24 So when you look at those embodiments in Figure 3 and Figure 4, all their
25 pores, all their complications, they all go away. They all disappear. There's

1 no barrier anymore at all to applying this well-known conventional
2 technique, okay?

3 Let me try to go back to make sure we hit all the other points I want to
4 hit on ligation. You know, the obviousness argument here is actually -- the
5 path forward is straightforward. A POSA would have been motivated to use
6 McCloskey's barcode with Linnarsson to avoid amplification bias. There's
7 only a small number of ways to introduce the barcode. That's what Dr.
8 Cooper said. There's only a small number of ways to do it. That's on Slide
9 148. You synthesize it together in one go from the outset, or you prepare it
10 separately, a molecular barcode, and you attach it to the first by ligation.
11 Those are the only two ways you can really do it. And ligation was a routine
12 and conventional approach. And then Dr. Cooper explains that ligation
13 offers a clear flexibility benefit. It's a benefit that you don't have to make the
14 full tag to the outset. You can choose how many tags you need and you can
15 ligate it on during the course of your experiment. Is it a huge, earth-shaking
16 benefit? No. But it's an approach that might help you with your workflow.
17 And so the path is really straightforward. When you have a clear motivation
18 to combine, only a small number of ways you can proceed, there's a routine
19 and conventional one that's on the table and it offers to the benefit. That's
20 the recipe of obviousness. There's two cases to look at. One is the Uber
21 case on Slide 152. The other one is the *Ball Aerosol* case on Slide 156.
22 Both of those, I think, are right on point relative to this case.

23 Now, the last topic I want to hit real quick is this notion of whether
24 McCloskey is prior art. They spent a lot of time on this. The key thing to
25 note here is that in the *Hulu* case, a precedential panel opinion was clear that
26 if there's a challenge to a reference status as a written publication, you can

1 submit a supporting declaration with your reply. We did that. This
2 testimony, it's not hearsay. They keep making a hearsay argument. Her
3 testimony is not hearsay. It's in-court testimony that's never been
4 challenged, and it shows that this was publicly available, and that it's prior
5 art, and it's not untimely. This is allowed pursuant to Hulu. It's allowed
6 pursuant to the Federal Circuit's *Vidstream* case on Slide 170. And if you
7 want to look at a case that really, really on point, another panel opinion, take
8 a look at the *Grunenthal* case on Slide 172. This case is a little different
9 from what they're proposing now. And the notion that McCloskey hasn't
10 been shown to be prior art -- this is a publication. It's got 2007 all over it. It
11 comes from a reputable publisher. There really can't be any question that
12 this is prior art. And with that, I don't want to cut into more of my rebuttal
13 time. I'll go ahead and stop there and take any questions before turning it
14 over.

15 JUDGE FITZPATRICK: Thank you. I think we'll proceed with Mr.
16 Baughman.

17 MR. BAUGHMAN: Thanks, Your Honor. Counsel, if you could
18 stop sharing. I have to confess to the Board, I don't intend to attempt that so
19 I'll just have to call out slides, and I think Your Honors have them available,
20 if that's all right.

21 JUDGE FITZPATRICK: We do have them. We have a PDF of them
22 and we'll assume you're talking about yours unless you specifically mention
23 that their Petitioner's.

24 MR. BAUGHMAN: Yeah. We'll call out both sets as that comes.
25 And if I could, Your Honor, we'd like to reserve five minutes of our time for
26 surrebuttal.

1 JUDGE FITZPATRICK: Done.

2 MR. BAUGHMAN: Thank you. May it please the Board. I'm Steve
3 Baughman, again, from Groombridge, Wu. And I'm with my colleague
4 Megan Raymond. We thank the Board for your time today on behalf of
5 10X. We'll try to address as much as we can with our time this afternoon
6 and flag some of the improper new arguments we've read and heard today.
7 We're also going to need to rely and stand on our objections, arguments, and
8 evidence that we put forth throughout the proceeding. That includes in our
9 slide objections, our objections to arguments, and paper 25 throughout our
10 substantive papers, and our motion to exclude.

11 Just to propose a roadmap for how we would plan to spend our time.
12 Obviously, we'll answer the questions the Board has as a priority. But I'm
13 going to propose to make some brief introductory remarks including about
14 the improper new arguments that we've had to confront. I will address
15 aspects of McCloskey. Then I'll ask my colleague, Ms. Raymond, to address
16 issues relating to the baselines and reference, including sequencing in
17 Ground 2. But obviously, we'll do that if Your Honors have questions in
18 other sequences, we will them up that way. And if time permits, we'll
19 address some other topics. I just recognize the Board has our briefing, and
20 we all have more slides that we can possibly go through in one hour.

21 We've already heard a lot throughout the proceeding and today about
22 things that, I think as Your Honor noted, are not in the grounds of this
23 Petition. You've heard a lot about inventions like the reflex method. The
24 idea of a specification disclosing multiple inventions isn't new to anybody in
25 the patent world. We've heard about the BD litigation concerning patents
26 that are not before the Board. They are not included in any ground by

1 Petitioner. If they had wanted to, they certainly could have, except, of
2 course, that they aren't actually prior art. And we've heard a lot of questions
3 that Petitioner asked of Dr. Quackenbush about issues that were not raised in
4 the Petition or in Dr. Cooper's opening declaration, and didn't come into play
5 until Petitioner belatedly and improperly raised them for the first time in
6 reply. These are questions that basically amount to hey, Dr. Quackenbush,
7 can you help me change my theory? And hey, Dr. Quackenbush, did you do
8 the work that I didn't do and maybe help me carry my burden as Petitioner?
9 As you are listening to the Petitioner today and reading their slides we'd ask
10 the Board to remember that Dr. Quackenbush has never had a chance to
11 respond to most of these arguments because they did not come up until
12 reply. And if you read the papers in this case sequentially from the
13 beginning -- I know there are many ways to tackle a pile of paper this big -- I
14 think that becomes quite clear. If you follow from the Petition onward,
15 you'll see how the arguments evolve and fall away for Petitioners. We've
16 heard a lot about arguments that basically boil down to this: put these two
17 references in a bucket and that's enough to show obviousness. A person of
18 skill could figure it all out. It could do this. It could do that. You could do
19 the other. That is not the law of obviousness. That is not how the Board in
20 this process requires parties to proceed as we're funneling down in an
21 expedited process. The *Intelligent Bio-Systems* case we've cited to Your
22 Honors absolutely requires much more than that. Petitioners are obligated to
23 say how and why a person of skill would have modified the references they
24 present, not just well, a person of skill would know what to do. The
25 *ExtractionTek* case we've cited Patent Owner response at 44 is a good
26 example. What modifications, what parts, of each of these references are

1 used and how, it's been black letter law that that's a requirement of the
2 reasoning and motivation that's been needed since *John Deere*. Now, when
3 Petitioners argue a particular theory for a motivation to combine, that also
4 has to be something that works, or it is not going to give a motivation to a
5 person of skill. And, again, that's the *Intelligent Bio-Systems* case, it's pages
6 13 and 67 to 69. We cite it on page 36 of our POR. I think the *Virtek* case is
7 also something that gets raised by the way counsel opened this morning --
8 this afternoon, excuse me. You have to explain and justify it even putting
9 together known elements. You can't just say it's conventional. That's not
10 enough. You have to specify a motivation. *Virtek* confronted and rejected
11 just this kind of argument. Simply put, the Petitioner has not done this. You
12 don't have to take our word for it. If you look at the Petition and Exhibit
13 1002, Dr. Cooper's opening declaration, you will see what their argument
14 was. And it's clear from their reply where they're disavowing their own
15 statements, dumping Petition arguments and starting over, arguing things
16 like obviousness modifications to hug which isn't even a reference in their
17 Petition. You know that they are starting over and that deprives us of due
18 process and violates the Board's most basic rules. The *Sirius XM* case at 15,
19 which we cite to Your Honors, is really informative on that point. And just a
20 little decoder ring tip, when you hear Petitioner say hey, that's not what the
21 claims require, it's really just code for Petitioner saying it's throwing out its
22 own theory the case. Like its own arguments for a motivation to combine.
23 Tagging all the polynucleotides in the sample, that's not our argument, it is
24 not a claim construction that Patent Owner is putting forward. It is
25 Petitioner's theory for what is needed to solve amplification bias. It is the
26 reason they gave Your Honors in the Petition for combining --

1 JUDGE FITZPATRICK: Mr. Baughman?

2 MR. BAUGHMAN: Yes, Your Honor.

3 JUDGE FITZPATRICK: Could you -- ultimately I'm going to ask
4 you a claim construction question. But first can you show us where they
5 take that position?

6 MR. BAUGHMAN: Yep. Yes, Your Honor. So if we turn to our
7 Slide 35. So Petitioner and Dr. Cooper asserted that a person of skill would
8 have been motivated to modify Linnarsson to, quote, solve amplification
9 bias by tagging each every and substantially all mRNA molecules and
10 Linnarsson using McCloskey 's teachings of a second tag. They set it up this
11 way. And I'll come to actual quotes in papers that Mr. Walter was asking
12 about. Linnarsson they say tees up a problem with amplifying the DNA.
13 But it doesn't solve it. It just reduces it. That's their premise. They say
14 McCloskey provides the exact solution by incorporating a second tag in an
15 oligonucleotide that uniquely identifies each sample polynucleotide prior to
16 amplification. McCloskey solves this source uncertainty problem for DNA
17 sequences generated by standard PCR. That's the Petition at 53 to 54, and it
18 cites paragraph 191 of Dr. Cooper. Fortunately for us, that's on a slide from
19 Petitioner. So if you look at Petitioner's Slide 59, they have highlighted that
20 McCloskey provides a direct solution to this problem amplification bias.
21 What they don't highlight is what it is -- what they say it is. It is using
22 barcodes to measure true sample complexity and template diversity. And
23 then it goes on to say by tagging each sample polynucleotide uniquely, true
24 sample complexity can be analyzed because each unique sample sequence
25 can be identified by the tag and amplification bias can be accounted for.
26 They're making a counting argument. You can see it on their Slide 55 and

1 on their Slide 58. If you look at paragraph 92 of Dr. Cooper's opening
2 declaration, Exhibit 1002, he's explaining this amplification bias process,
3 and he cites to McCloskey, page 6. He says here's how you solve it. Quote,
4 every sample and the polynucleotides within every given sample are first --

5 JUDGE FITZPATRICK: Mr. Baughman?

6 MR. BAUGHMAN: Yes, Your Honor.

7 JUDGE FITZPATRICK: I'm sorry. I'm pulling that up right now.
8 What can you tell me the source document?

9 MR. BAUGHMAN: Yeah. I'm sorry, Your Honor. It's Exhibit
10 1002.

11 JUDGE FITZPATRICK: Yep.

12 MR. BAUGHMAN: It's page 40, paragraph -- I think it's PDF page
13 45 in the numbers in the lower right. Paragraph 92.

14 JUDGE FITZPATRICK: I'm almost there.

15 MR. BAUGHMAN: Yes, Your Honor. I'm sorry. I should have
16 tried displaying the slides.

17 JUDGE FITZPATRICK: No worries. I'm there.

18 MR. BAUGHMAN: Okay. It's talking about solving the problem,
19 that's what it starts out with on 92. That's the amplification bias that's talked
20 about on 91. And it says -- and McCloskey is Exhibit 1004 -- .006 is page 6
21 of McCloskey. Every sample and the polynucleotides within every given
22 sample are first uniquely tagged before being amplified and thereafter
23 sequenced. By uniquely tagging the sample and the polynucleotides,
24 researchers can track the number of polynucleotides in their source by
25 counting the number of unique tags. And you skip to the last line. This
26 results in addressing amplification bias by keeping a track of the

1 polynucleotides in the original sample. So we're not making this up. Where
2 did we get it? We got it from Dr. Cooper in the Petition at 54 and 53. Now
3 --

4 JUDGE FITZPATRICK: Let me push back a little bit on that
5 because part of what flavors this is the word sample. So if sample doesn't
6 mean all of the polynucleotides -- in order -- if I tagged each sample
7 polynucleotide but only two are required of the claim, then I don't have this
8 problem. Is that fair?

9 MR. BAUGHMAN: Yes, Your Honor. And I think that -- I was
10 going to come to that at a higher level. The claims don't require this, but
11 their theory does. In order to detect amplification bias, you need to be
12 tagging substantially all of the mRNA. That's what --

13 JUDGE FITZPATRICK: I think that each time -- okay. So for
14 example, in paragraph 92, they talk about by uniquely tagging the sample
15 and the polynucleotides, researchers can track the number of polynucleotides
16 in their source by counting the number of unique tags. For example, that
17 sentence does not say what you just said. Is there a sentence that says what
18 you just said?

19 MR. BAUGHMAN: The sentence that says what I just said is the
20 one we quote on the last bullet of 35, which is where Dr. Cooper admits that
21 Linnarsson describes a method which is designed to be applied to
22 substantially all mRNA molecules of the cell. Okay? So the sample is
23 supposed to be substantially all -- this is what they've put together. The base
24 reference is Linnarsson. Tag substantially all of them, and then for each
25 sample and every polynucleotide in it, uniquely tag. That's what they say.
26 And by the way, I heard Mr. Walter. They can change their theory of the

1 case based on something that happens in another IPR. We are absolutely
2 allowed to take admissions from what Parse has said elsewhere. But they
3 can't take an opinion that Dr. Cooper gave somewhere else.

4 By the way, I think it's super enlightening that Dr. Cooper elsewhere
5 gave an opinion realizing a need to expand this tag. I challenge Petitioner to
6 find in the declaration where he talks at all about expanding the tag before it
7 comes to the reply declaration. It's a 7-nucleotide tag. I can come to that
8 more detail in a minute. But this whole idea that they get to say well, what
9 we're quoting here is from another IPR, because it's what Dr. Cooper
10 admitted about Linnarsson. Linnarsson's the same. But he doesn't get to
11 make an obvious to go to 20 or 30 nucleotides argument here for a tag.
12 That's nowhere in the Petition. And he can't say well, because you cited an
13 admission I make, I get to bring in all the theories that used somewhere else.
14 Coulda, woulda, shoulda. That is not what we get to respond to on reply and
15 Dr. Quackenbush can't opine about it. So, Your Honor --

16 JUDGE FITZPATRICK: In this other case describing what
17 Linnarsson -- whatever Linnarsson says, I get that whether it's a different
18 proceeding. But this statement -- this last statement that -- and I'm looking
19 at Patent Owner demonstrative number 35.

20 MR. BAUGHMAN: Yes, Your Honor.

21 JUDGE FITZPATRICK: That is characterizing what Linnarsson
22 describes. How do you get from that to saying this is a characterization of
23 the motivation of what -- this is what Petitioner articulated as the
24 motivation?

25 MR. BAUGHMAN: If you look -- and let me find the Petition pages,
26 Your Honor. They're arguing now as an example that you can just do some

1 of the cells. I think our Slide 43 addresses this. In order to actually solve
2 amplification bias instead of reduce it, you need to do what they're saying
3 which is to count these -- count everything. If you look at Petition page 54
4 and, Your Honor, if you want to turn there I'll wait until the people pull it
5 up. It's Paper 1, page 54 of the Petition.

6 JUDGE FITZPATRICK: I'm there. I'm there now.

7 MR. BAUGHMAN: Okay. Midway down the page on the right it
8 says Linnarsson attempts to address the problem of amplification a certain
9 way. Then at the bottom of that paragraph it says this approach only reduces
10 amplification bias, it does not actually solve the problem. McCloskey,
11 however, provides the exact solution. And it's by incorporating a tag that
12 uniquely identifies each sample polynucleotide prior to amplification. It
13 doesn't say in the sample. It says each polynucleotide prior to amplification.
14 McCloskey solves it. That's their theory. That's what we responded to, and
15 it is unfair to come up with some new theory now that we don't have an
16 expert to talk about. I mean, I recognize that Petitioner's job here is to -- I'm
17 going to list, if Your Honors have the time for it, a number of really
18 foundational points on which the reply completely changes course, and we
19 find ourselves responding to arguments, why didn't you talk about that?
20 Because it wasn't in Dr. Cooper's testimony before. If I could just quickly --

21 JUDGE FITZPATRICK: Wait a second.

22 MR. BAUGHMAN: Yes, Your Honor.

23 JUDGE FITZPATRICK: Before we leave this, do you have a claim
24 construction about sample polynucleotides? Does it read on two
25 polynucleotides? Can you have a situation -- okay. Go ahead.

1 MR. BAUGHMAN: I haven't -- to be honest I'm not on the litigation
2 side. I haven't looked at the outer limits of what it doesn't or doesn't require,
3 so I don't want to state a position one way or the other. I didn't think it
4 matters. Because, again -- and this is what happened in the *Intelligent Bio-*
5 *Systems* case as well. They argue the claim doesn't --

6 JUDGE FITZPATRICK: Let me explain to you why I think it might
7 matter.

8 MR. BAUGHMAN: Okay.

9 JUDGE FITZPATRICK: If the sample polynucleotides limitation
10 reads on just two, then you can reduce amp -- or you can solve, I guess, and
11 potentially -- amplification bias by uniquely tagging each of those two
12 polynucleotides before you PCR them, amplify them, and you will be able to
13 tell, I guess, the relevant ratio between those strands prior to having
14 amplified them, even if there is bias in how often they are replicated.

15 MR. BAUGHMAN: I guess I --

16 JUDGE FITZPATRICK: You might not have any information
17 relative to other polynucleotides that weren't part of the sample but were in
18 the cell, but between these two sample polynucleotides, you would have
19 information.

20 MR. BAUGHMAN: I have a couple reactions, Your Honor. And,
21 again, I haven't thought about this claim construction issue because we really
22 don't think a claim construction is needed here. You don't have -- you don't
23 know if you're tagging those two because Linnarsson tags randomly to begin
24 with. You can't target the polynucleotides here to say a particular gene
25 because that's not what Linnarsson does. And as we understand, at least the
26 original theory here, they're working with Linnarsson's cell tag, not

1 something from McCloskey where it's doing some special kind of targeting.
2 They're taking a random tagging of Linnarsson. It's not -- we don't know if
3 it's going to work. There's certainly no reasonable expectation. And the
4 whole idea in the *Intelligent Bio-Systems* case is saying what the claim
5 requires is one thing, saying what your theory of motivation is another. And
6 their theory is not about what the claim requires, it's about solving
7 amplification bias. That's the story they're telling you about why you take
8 McCloskey and slap it -- its teachings, and I'm not -- I don't want to say slap
9 but we're not saying bodily incorporation. They say take the function of both
10 of barcode and the batch-stamp, which we'll come to if there's time, and
11 apply them to these two segments of Linnarsson. And Your Honors, at
12 pages 21 and 22 of the institution's decision totally recognize that. We're
13 concerned that it was very difficult to understand what the theory was. Your
14 Honors said we can understand what the theory is. It is what is in paragraph
15 192 of Cooper. It is conceptually dividing the existing Linnarsson cell tag
16 into two pieces, applying the batch-stamp function to the first piece, and to
17 the 7 nucleotides that he talks about, applying the barcode to that second
18 piece. And I'm happy to come to more details. There are a couple higher
19 level points I'd like to make to Your Honors. But if you want to talk more
20 about substantially all I'm happy to do that or I can come back and hit some
21 other points.

22 JUDGE FITZPATRICK: No. Hit what you want to hit.

23 MR. BAUGHMAN: Okay. And to be clear, I want to hit what Your
24 Honors have questions about. So I'm not trying to stick to a script. I just
25 want to cover a lot of ground if it's useful. The other two examples I just
26 want to throw out, we have a handful of objections stemming from sort this

1 mega-footnote of page two of their reply where they -- there's a massive
2 string, it has, like, six lines of the brief where they just snippet cites to Dr.
3 Quackenbush where they basically asked him questions about things that
4 were not yet in play in this IPR.

5 Now, they've improperly taken that and turned into like 34 slides each
6 with a headline with things like does not know, no explanation, will not say.
7 If they wanted to make arguments about each of those snippets, they could
8 have done that in the brief, and we could have responded to them. You
9 know, throwing them out in slides now and saying oh, gotcha, gotcha,
10 gotcha. I just think it bears looking at and I encourage Your Honors to read
11 the Q and A that are into a lot of these snippets in the full context. One of
12 the things that caught my ear also -- and I know Ms. Raymond is going to
13 talk about it -- on Slide 36, they're suggesting that Dr. Cooper opined about
14 sequencing the entirety. And, again, Ms. Raymond's going to talk about this
15 more detail. Look higher up, in that same slide, Slide 36, the part they don't
16 highlight. He starts out by saying Dr. Cooper asserts the tagged
17 polynucleotides are the cDNA generated, that's how their mapping it. But
18 that's what gets sequenced. These type polynucleotides are sequenced. So
19 he's reading it right there. It's not something that came up in reply. It's right
20 there in the same paragraph of his original POR declaration. That's how
21 we've been reading their argument from the beginning. And the sort of idea
22 that they get to switch around and then claim that we knew all along, is just -
23 - it's not something we can deal with as a matter of fairness.

24 And then the other thing I want to just note is they mix in a lot of
25 arguments and citations from their motion to exclude briefing into the slides.
26 I know Your Honors know that's not merits briefing. And I know it'll get

1 sorted out correctly. But even this afternoon we've heard mixing of the
2 arguments on the merits for what's actually shown to be prior art versus
3 arguments about excluding are not, and we're happy to pick that up if there's
4 time.

5 Taking a look at the time here, I do think it's important to talk about
6 the range of things that are totally new here. We talked about several of
7 them already. On Slide 81, we would submit -- and I know Your Honors
8 hear about new arguments all the time -- but this is really, to my experience
9 a remarkable case, and the volume of out-of-scope arguments that are
10 showing up on reply here that we have to try to deal with certainly merit
11 what the Board has often done which is ignoring a reply with -- once you
12 find something new. And the trial practice guide -- we've got plenty of these
13 things. Everything that's listed here, new evidence, new rationales to
14 combine, you can find all of them in the examples I'm going to quickly go
15 through. We may need to stop on some and talk merits. On Slide 82, I'm
16 happy to talk about the 7-nucleotide point. It has absolutely been their
17 theory that this is a 7-nucleotide mapping until reply. And I'll come -- I will
18 come back to that, but if you want to talk about it now I can. Now they're
19 saying oh, it can go up to 4 to the end. They're arguing for 20 to 30, which
20 actually wouldn't even fit Linnarsson's original cell tag. If you look at Slide
21 83 --

22 JUDGE FITZPATRICK: Mr. Baughman, on the length of the cell
23 tag issue --

24 MR. BAUGHMAN: Yes, Your Honor.

1 JUDGE FITZPATRICK: -- your argument, limited to that, it's a new
2 argument? Or would you argue -- are you arguing that a person of ordinary
3 skill in the art couldn't do it? Wouldn't have known how to do that?

4 MR. BAUGHMAN: Well, they --

5 JUDGE FITZPATRICK: They make an argument -- I'm sorry. They
6 make an argument that they're -- of course the POSITA is not an automaton.
7 If he needs -- if he or she needs more unique tags, you just increase the
8 number.

9 MR. BAUGHMAN: Sure. Well, I think a couple --

10 JUDGE FITZPATRICK: That's a new argument. I get your saying
11 that, but is there -- what about substantively? Are they correct?

12 MR. BAUGHMAN: They're not correct because they haven't
13 explained how you would do it. So, for example, they're arguing -- and I
14 think it's actually the Slide we were just looking at --based on two pieces of
15 evidence that were not in the Petition, McCloskey 2 and this declaration
16 from another Petition that you could get to 20 to 30 nucleotides for the
17 barcode, right. Well, their theory is as to take Linnarsson's existing
18 sequence of 20, use a part of it for the batch-stamp, and use a part of it for
19 the barcode. So they're going to need to do some lengthening. And they're
20 going to need to go into an obviousness analysis of why you would do this
21 and how you would do this and what the consequences would be, and
22 they've done none of it. So it's a new argument. I'm not saying that we have
23 testimony one way or the other on this because it wasn't an argument where
24 we got to respond with an expert. But it's not only a new argument; it's a
25 new argument that isn't even explained. It's not a simple argument. And,

1 Your Honor, if this is a good time I'm happy to show why it is their
2 argument and they can't just walk away from it now.

3 JUDGE FITZPATRICK: Sure. Yeah. I know the citations to where
4 the 7 originates from. I'd be interested to know kind of the best case
5 scenario of how they boxed themselves into that.

6 MR. BAUGHMAN: Well, let's take a look at their slides here, Your
7 Honor. Parse Slide 21.

8 JUDGE FITZPATRICK: Did you say theirs or yours?

9 MR. BAUGHMAN: Theirs. So Parse Slide 21. They're calling the
10 yellow thing the barcode. It has 7 Ns, 7 nucleotides. Same on Slide 51. On
11 Slide 184, this is Parse's slides, Petitioner's slides. They've got the whole
12 figure now that they're using from McCloskey as their theory. This is what
13 they're arguing. They highlight it for you. They show you where it is. The 7
14 Ns are still there in the A section of this figure. But now let's look at F, G,
15 H, and I. Each of them has a 7-nucleotide barcode on the left. And it didn't
16 just come up in their slides. That's not just a mistake. It's in the Petition at
17 31, 35 and --

18 JUDGE FITZPATRICK: I get -- I think that you'll -- I mean, it's
19 obvious to me why they picked seven. That's because that's the example
20 that's used in the prior art reference that they're relying on. What's the best
21 argument for limiting them to that example? They say they shouldn't be. If
22 you look at the reference, it says we currently use seven, I believe I might be
23 misquoting -- something to that effect.

24 MR. BAUGHMAN: So the reference is actually --

25 JUDGE FITZPATRICK: Which suggests hey, maybe we'll use more
26 in the future, or someone could use more.

1 MR. BAUGHMAN: Yeah. And I think this goes back to *Virtek* and
2 all the case law that basically says something might be known. It might
3 have a tag that's known to be 7. There might be other tags that are known to
4 be longer. But you need to tell me that's what you're doing. And what they
5 told us they were doing was a 7-nucleotide tag. That's what we responded
6 to. And they haven't said what implications something longer than 7, would
7 have for the entire rest of the claim and the mapping in Linnarsson.

8 JUDGE FITZPATRICK: So it sounds to me, the response -- the way
9 that they boxed themselves in is that it's not that the reference doesn't
10 suggest that you could use a different length. It sounds like you agree with
11 that. But that they, Petitioner, didn't make that argument. And that's
12 exclusively why they couldn't do it with 8 or 9 or 10.

13 MR. BAUGHMAN: I'm sorry, Your Honor. Not only did they not
14 make that argument, but they didn't explain what impact, if any, it would
15 have on their combination, and that's part of their obligation to do. And I
16 think --- I'm trying to find the slide now. The fact that they are relying now
17 on their testimony in another IPR where they did account for this, where
18 they did say hey, instead of just citing it to 7 --and by the way we have
19 testimony from Dr. Cooper acknowledging that the only thing he cited in his
20 declaration was the 7. He never quoted the 4 to the end formula or anything
21 else. And in another IPR that's what they went off and did. He said well,
22 here's 4 to the end. I lay it out. Here's how I could -- here's why it would be
23 obvious to expand that. What we're missing here is an obviousness
24 argument. Why would you change the 7 that you relied on in McCloskey to
25 make it more? Why would that be efficient? Why would that make sense
26 instead of doing something else with what's already in Linnarsson? And we

1 don't have any opportunity to respond to that with our expert because this
2 didn't pop up until reply.

3 Your Honor, I'm happy to keep going on the 7, but there's obviously
4 more to say. On 83, again, McCloskey 2 and Dr. Cooper's new declaration
5 are not evidence in this matter. Although they do -- I'll just point out on
6 Slide 79 and 80 that Mr. Walter just showed you, those are evidence that
7 was not in the Petition. He's relying on McCloskey 2 for the top of
8 Paragraph 85 on Slide 79, and he's relying on his old -- his declaration in
9 another matter at the bottom of that paragraph. How do we know? Look at
10 Slide 80, that's the declaration from the other matter. So you want to find a
11 new argument, he put it on a slide.

12 JUDGE FITZPATRICK: Mr. Baughman, I'm on Slide 79
13 Petitioner's, and can you repeat what you just said? I see he's citing to the
14 reply declaration which I understand, you know, is a reply declaration.

15 MR. BAUGHMAN: Yes, Your Honor.

16 JUDGE FITZPATRICK: What did you say about the source
17 document? That it's being cited within this?

18 MR. BAUGHMAN: Yeah. So Paragraph 85 at the top it says the
19 McCloskey Patent Application and it gives a number, that's McCloskey 2.
20 It's not -- it was not cited in the Petition. Okay. So he's using that to show it
21 would be obvious to comprise 20 to 30 random nucleotides.

22 JUDGE FITZPATRICK: Had you cross-examined him as to whether
23 or not that was true?

24 MR. BAUGHMAN: I don't -- I honestly don't recall. We might
25 have.

1 JUDGE FITZPATRICK: You had the opportunity to cross-examine
2 him, and they're allowed to rely on stuff to give us their opinion.

3 MR. BAUGHMAN: Well, this is a new theory. They never argued a
4 20 to 30 nucleotide barcode before, and we didn't have an expert with an
5 opportunity to respond to this. I have to go look at the deposition to see if I
6 asked about that. I may have asked about whether it was new. And it's a
7 new reference that's certainly not part of their prior art combination. I don't
8 think that the Board authorizes obviousness combinations with references
9 that appear for the first time in reply. Similarly, I don't think the opinions in
10 Exhibit 2011, which he cites in the last line of this box, is fair game for
11 Petitioners to change their theory now and add an obviousness opinion
12 which is on Slide 80. A person of skill -- this is their opening -- this is a
13 Petition argument on Slide 80. A person of skill would have found it
14 obvious to design something using the 4 to the 9 formula. That is nowhere
15 in the Petition here. It's brand new evidence from another IPR, and it's
16 certainly illustrative of what we've been dealing with here. I'm just going to
17 quickly tick off some others, Your Honor. Counsel noted on Slide 84 --

18 JUDGE FITZPATRICK: Mr. Baughman, how would they -- I just --
19 there's a chicken and egg problem here. You're saying that this is a new
20 argument. But they're responding to your argument that the label wouldn't
21 be big enough. A label of only 7 wouldn't be big enough to have enough
22 unique combinations to cover all the sample polynucleotides, even though
23 both sides seemingly agree that only two sample polynucleotides is
24 sufficient for the claim. Setting that aside, you made this argument, they're
25 responding to that. And if -- I mean, I think fairness goes both ways. How

1 do you -- try to explain, I guess, that to me. I'm trying to understand how
2 that's not fair.

3 MR. BAUGHMAN: Absolutely, Your Honor. They are absolutely
4 allowed to say -- when you criticize me for something I said in the Petition, I
5 can show you why you're wrong, why the Petition is right. So I can show
6 you why 7 nucleotides is fine. You're imagining that. And I'm going to
7 come to that. They argue -- they made up new arguments about bacteria and
8 yeast, both of which are also sufficient -- insufficient in number to cover
9 what they say you need to have for tagging. They both fail. But they're
10 entitled to come up with oh, here's an excuse why the Petition -- or an
11 explanation why the Petition was right. What they're not entitled to do is oh,
12 you show I was wrong, here's a twist on the Petition. I'm going to change
13 my theory. It's no longer a 7-nucleotide barcode, it's a 20 to 30 nucleotide
14 barcode, longer than what I said I was going to use. Longer than
15 Linnarsson's original cell tag that I say I'm going to conceptually divide and
16 use part of it as the barcode. I'm going to exceed that, and who knows what
17 else I might change if you ask another question. You don't get to change
18 your theory, you get to show why your theory was right. And you can cite
19 additional evidence to show why your original theory was right, not why a
20 new theory you just made up will work.

21 JUDGE FITZPATRICK: I understand that conceptually. I don't
22 know if that is an accurate characterization of the back and forth in this case.
23 I think, in your view, you want us to believe that Petitioner's obviousness
24 ground hinged on using -- exclusively -- on using a 7-character long label for
25 the second tag, using it only for mammalian cells and using it only where the
26 sample polynucleotides meant all the polynucleotides. And I don't see -- I

1 think all 3 of those things are fair of the position you're taking about what
2 Petitioner -- you know, in characterizing the position Petitioner is taking.
3 But I don't see that Petitioner took that position.

4 MR. BAUGHMAN: Okay. I'll briefly revisit that. So as we talked
5 about, in their Petition, they explain that they solved the problem of
6 amplification bias by tagging everything. And that past passage I read from
7 the Petition is not limited to sample, Your Honor. That's what they say.

8 JUDGE FITZPATRICK: I would doubt they said that because of the
9 tense of what you've just said. So I want to be specific. They didn't -- I don't
10 think they said they solved it, right. If they're talking about the person of
11 ordinary skill in the art they probably said would have solved. But I asked
12 you this before. I would like you to you take me to some place in the record
13 where they say that. Not in your slide that cites to the record, they do have
14 accurate cites to the record. I don't want to do a two-step process. I'd like to
15 go -- you can use the slide for your benefit, but take me to a document in the
16 record where they take that position about the motivation -- not about what
17 Linnarsson teaches or what Linnarsson describes, but about the motivation
18 for the combination for the modification.

19 MR. BAUGHMAN: The motivation, Your Honor, is discussed on
20 page 54 of the Petition. And they --

21 JUDGE FITZPATRICK: Let me get there, please.

22 MR. BAUGHMAN: Yes, Your Honor.

23 JUDGE FITZPATRICK: Okay. Okay. I'm there.

24 MR. BAUGHMAN: So taking it a step at a time. The quote on 35
25 about Linnarsson being designed to be applied to substantially all mRNA
26 molecules of the cell, that's something that --

1 JUDGE FITZPATRICK: I'm sorry. Did you just reference -- did
2 you just reference -- just focus on this page, please, or whatever page you
3 want.

4 MR. BAUGHMAN: So I'm on page 54 of the Petition. Linnarsson
5 attempts to address amplification bias in one way, but only reduces
6 amplification bias. That's what they say. This approach only reduces
7 amplification bias, and it does not actually solve the problem. McCloskey
8 provides the exact solution by incorporating a second tag in an
9 oligonucleotide that uniquely identifies each sample polynucleotide prior to
10 amplification. And that is an improvement of using McCloskey to improve
11 Linnarsson. And what Linnarsson teaches according to Dr. Cooper is
12 another document that I can take you to.

13 JUDGE FITZPATRICK: But I don't think that gets you there,
14 because that sentence says incorporating a second tag and a oligonucleotide
15 that uniquely identifies each sample polynucleotide prior to amplification.

16 MR. BAUGHMAN: And what --

17 JUDGE FITZPATRICK: So --

18 MR. BAUGHMAN: Sorry, Your Honor.

19 JUDGE FITZPATRICK: Okay.

20 MR. BAUGHMAN: You need to know --

21 JUDGE FITZPATRICK: Yeah.

22 JUDGE FITZPATRICK: And where do you get all? How do you
23 get all?

24 MR. BAUGHMAN: We get that because Dr. Cooper also says --
25 testifies under oath that Linnarsson describes the method which is designed
26 to be applied to substantially all mRNA molecules of a given cell. That's not

1 limited to a sample. So we know something -- we know what the sample is
2 based on what Linnarsson teaches. We start with Linnarsson which is
3 designed to tag everything, so the samples in Linnarsson are designed to tag
4 everything, and then we take the sample and tag everything in it. That's
5 what this motivation says. And the only way you get to count the number of
6 -- you can also look at the opinions of Dr. Cooper about being able to
7 actually count and get diversity -- true diversity numbers. How do you
8 know what the diversity of molecules in a cell is -- can be some
9 polynucleotides that only show up a few times according to Dr. Cooper.
10 How do you get that without actually tagging everything or substantially
11 everything? That's where the quotes are coming from.

12 JUDGE FITZPATRICK: Okay. I think I understand your position.
13 Thank you.

14 MR. BAUGHMAN: I think I might need to abbreviate this a little bit
15 and pass it to my colleague in a moment. I guess the one other thing I would
16 say is: I urge Your Honors to look at our list of new arguments. They are a
17 lot of very substantial and important ones that I haven't had a chance to talk
18 about that we think are quite clearly shown in the papers. And I guess the
19 one other thing I want to mention for a moment is on Slide 45. This is their
20 first tag theory. So they map Linnarsson for claims 1-E and 1-H to
21 Linnarsson's original cell tag, its own cell tag, for the first tag sequence.
22 Then relying on Dr. Cooper for limitation 1-F where they start talking about
23 the second cell tag, they bring in the batch-stamp functionality language
24 we've looked at several times now in Paragraph 192 of Cooper's declaration
25 that the institution decision picked up at pages 21 and 22. It's conceptually
26 divided into two portions. The first portion performs the function of the

1 batch-stamp. We recognized that, the Board recognized that, and now in
2 reply, Petitioner's trying to say well, it's clear that that was never there.
3 That's never what they mapped. And that's exactly the mapping the Board
4 relied on to institute. So there are two problems there. First, they're
5 switching what they're relying on as the first tag and that's a violation --
6 basic mapping of a claim, *Netflix* talks about that, the *Netflix* case. And it
7 also fails on the merits because McCloskey's batch-stamp doesn't function as
8 a cell tag. It doesn't distinguish among cells, it does the opposite. And
9 lumps all cells in a sample together. They're all lysed and only tagged after
10 they're mixed. And the notion -- it's also outside the claim to sort of say a
11 sample of just a single cell. That's not -- the claims require multiple cells in
12 the sample. So they're mixed together and then only after that are they
13 tagged. So the batch-stamp from McCloskey does not work and it's also
14 switching what they're mapping. Unless Your Honors have questions I think
15 I'll pass the podium to my colleague, Ms. Raymond.

16 MS. RAYMOND: Good afternoon, Your --

17 JUDGE FITZPATRICK: Good afternoon.

18 MS RAYMOND: Good afternoon, Your Honors. May it please the
19 Board. Hopefully, my audio is now working. I'm Megan Raymond of
20 Groombridge, Wu, Baughman and Stone, for Patent Owner. I'll plan to start
21 by addressing the sequencing limitation including Linnarsson's disclosure
22 and Petitioner's reliance on fragmentation and capture, including the issues
23 and arguments about Figures 3, 4, and 11, and examples 1 and 2; and then
24 move on to Ground 2 which is the ligation claim, Claim 5, unless Your
25 Honors would prefer a different order.

1 With respect to the scope of the claims and sequencing -- the
2 sequencing limitation, we are not asking for construction that the claims
3 require sequencing the entire polynucleotide. We aren't construing the
4 claims to require that the entire polynucleotide is sequenced. Instead, their
5 argument -- Petitioner's argument for obviousness in the Petition requires
6 that the entire polynucleotide be sequenced. We're asking that Petitioner be
7 held to their mapping in the Petition, and they don't get to switch what
8 they're mapping between the Petition and the reply. And I point you to Slide
9 -- Parse's Slide 36 which Mr. Baughman pointed out as well and the
10 statement that Dr. Cooper asserts that the tagged polynucleotides in
11 Linnarsson are the cDNA generated during reverse transcription, and that, in
12 his opinion, these tagged polynucleotides are sequenced. So Dr.
13 Quackenbush's understanding of their theory was that these tagged
14 polynucleotides are sequenced and that's when -- when he was deposed in
15 February of 2024 he didn't need to have determined whether the claims
16 require it, he was looking at what Dr. Cooper theory was. Even if they're
17 allowed to present their new theory on reply, they haven't shown that enough
18 of the tag is sequenced -- or enough of the tagged polynucleotide is
19 sequenced, excuse me. And I don't think that they have any showing that
20 they're being consistent with the district court -- just as an aside, I know that
21 there's a lot that's not of record here, a lot that's gone on before, but I just
22 note, you know, we have what we have from the district court and nothing
23 else about what their positions have or haven't been. Going into sequencing
24 itself, Petitioner's arguments focus on whether Dr. Quackenbush interpreted
25 the claims to require sequencing the entire polynucleotide, but the dispute
26 again is not about the claim construction, it's about whether Petitioner

1 proved what's in its Petition. If we go to our Slide 25, the Petition and Dr.
2 Cooper said that the sequencing limitation is met because Linnarsson
3 teaches sequencing the entirety of the tagged polynucleotide and specifically
4 what they said is that Linnarsson teaches that after generating the tagged
5 polynucleotides, sequencing is performed thereon. They didn't say it was
6 performed on, you know, a piece of the tagged polynucleotides. They said
7 sequencing is performed thereon. And, again, I've read you Parse's Slide 36.
8 And I'm going on from there in response, Patent Owner in the POR and Dr.
9 Quackenbush explain that Dr. Cooper mischaracterized Linnarsson and that
10 Linnarsson doesn't teach sequencing of the entire polynucleotide, not that
11 the claims require sequencing the entirety of the polynucleotide. And then
12 on reply what happened was that Petitioner argued Quackenbush improperly
13 construed the claims to require sequencing of the entire polynucleotide,
14 which is interesting since, of course, Dr. Quackenbush specifically said he
15 had not construed them. That was in February of 2022. Come May 2022 --
16 or, excuse me, February 2024 come May 2024 in the district court litigation
17 he had then performed a construction. So Petitioner is now trying to say
18 there's an inconsistency, but really what's happening here is simply a
19 response to the arguments that were made.

20 JUDGE FITZPATRICK: Dr. Quackenbush's construction now is
21 what? About how much needs to be sequenced?

22 MS. RAYMOND: I think, I mean there hasn't been -- I don't think
23 we've seen a construction from the Petitioner. Dr. Quackenbush in the IPR
24 has not provided a specific construction, but in the litigation I think that
25 construction is simply that the entirety of the tagged polynucleotide -- no,
26 there's no construction. Sorry. There's no construction in district court, but

1 Dr. Quackenbush has said that the entire polynucleotide need not be
2 sequenced.

3 JUDGE FITZPATRICK: Yeah, I saw -- we saw the claimed
4 construction order that was submitted. If I can -- it involved multiple
5 patents, two families, Brenner and something else -- and of which the '981 is
6 a Brenner. But I didn't see this phrase construed by the court there. But did
7 Patent Owner take a position -- did Patent Owner advocate for a
8 construction?

9 MS. RAYMOND: I think that -- I don't think that there was a
10 construction per se that was set forth, but, you know, of course Dr.
11 Quackenbush said that the entirety need not be sequenced. But enough does
12 need to be sequenced such that the tags and the sample sequence can be
13 identified, and the tag's function -- the tag's function can be performed. So,
14 you know, if you only -- sorry. Go ahead.

15 JUDGE FITZPATRICK: Would that be -- I mean I understand your
16 position in this case that you don't officially have a construction on that, but
17 is that -- is that -- would that be today your construction? If I said I need a
18 construction from your right now, is that the construction?

19 MS. RAYMOND: The construction would be enough needs to be
20 sequenced such that the tags in the sample sequence can be identified, and
21 the tags -- can tag's function can be performed. So you would need to be
22 able to tag -- you'd need to sequence the tag --the tags, right, and you would
23 need to sequence enough of the original sample polynucleotide that you
24 know what you're looking at. And one of the issues here is even once
25 Petitioner has sort of changed its position and said, oh, you can sequence

1 only a subset, they haven't said how much of that subset is sequenced and
2 whether enough of it is sequenced.

3 JUDGE FITZPATRICK: Even if you had to speculate, please do.
4 Why would they -- why would in the prior art they do sequencing thereon if
5 they weren't getting enough data?

6 MS. RAYMOND: I mean, I think we've turned this from Linnarsson
7 where Linnarsson's looking at tagging, you know, tagging things particular
8 to just the cell and now we've moved on to wanting to know information in
9 particular about, you know, every polynucleotide in the cell and being able
10 to distinguish every polynucleotide in the cell and tagging those and looking
11 at whether those are different and being able to count them up and see
12 differences. So, you know, I think -- and it also creates issues of where the
13 two tags are once you get -- once you make a combination, are the tags next
14 to each other? Are we, you know, with ligation are the tags not next to each
15 other? So we need to be able to tag -- you know, we're not talking about
16 really Linnarsson itself, we're talking about whether combination is going to
17 sequence a sufficient amount to sequence the tags in enough the sample
18 polynucleotide that we know what we're talking about here. Of course, the
19 burden is on the Petitioner. They need to make that showing to meet the
20 claims and they haven't explained that.

21 JUDGE FITZPATRICK: What if we stick with -- let's assume the
22 seven -- the seven digits of the label, right. And that -- I forget what the
23 native Linnarsson tag is. The total might be 15, right. They say we'll use
24 eight for the first and seven for the second function. I can't remember. Let's
25 just assume it's 15 for this. And, and your position is that Petitioner's not
26 changing the length of that. They're going with what it -- with what the

1 example that's disclosed in the prior art and they're not changing its length.
2 So in Linnarsson, in native Linnarsson, they would -- this description of
3 sequencing performed thereon, that is sequencing the tag which is the same
4 number of nucleotides whether it's modified in view of McCloskey or not in
5 my hypothetical. Then they would also have to -- for Linnarsson to work,
6 and presumably it does -- Linnarsson would also have to sequence part of
7 the polynucleotide to which the tag has been attached. So -- and they would
8 presumably be doing enough of that polynucleotide to make the information
9 be useful. So why wouldn't -- if you make the modification and it would just
10 stick with the conceptually dividing, right -- we're not actually changing the
11 length of the native Linnarsson tag. We're just focusing for two functions
12 now, and then the sequencing is perform -- is quote performed thereon
13 unquote. Why wouldn't that be enough sequencing?

14 MS. RAYMOND: So I think -- I mean -- and I'll set aside Ground 2
15 because the tags may be separated in different ways and focus, I think, on
16 your question which is really limited to Ground 1. And in terms of the
17 sequencing itself, again, I think the -- how much of the polynucleotide you
18 need, I think, has -- there's no evidence in here of how much you would need
19 once you are looking at and needing to compare one polynucleotide from the
20 combination to another. So in -- again, in Linnarsson itself if you've tagged
21 -- tagged each polynucleotide in the cell you're just looking at, you know,
22 each polynucleotide sort of what -- you know what is in each cell, but you
23 don't know anything about the details of each polynucleotide. Now, we've
24 added a tag to tell us how many polynucleotides we have so that we can get
25 details about those polynucleotides. I don't know whether you would need
26 additional length of the polynucleotide in order to be able to sufficiently tell,

1 oh, I have two different polynucleotides here because, you know, there's a
2 mutation -- base point mutation here and not here. Your Honor, I'm sorry.
3 You know, I just don't know the answer to that because it's not something
4 that came up until late in the case so we don't have, you know, we don't have
5 an expert on it.

6 JUDGE FITZPATRICK: Understood. Thank you for that.

7 MS. RAYMOND: So I want to get -- I want to make sure I can cover
8 a bit the Figures 3, 4 issue et cetera. So I'll just quickly mention Petitioner's
9 citations in the Petition regarding sequencing. They have 3, 3 cites only.
10 They don't say what sequence with respect to the first two cites. Their third
11 cite, they rely and emphasize that the cDNA library is sequenced. I would
12 note that the cDNA library is defined as fragments but that I have sort of
13 pushed back on that in this proceeding. And what they don't cite in their
14 Petition are the citations in Linnarsson that refer to the 3 -- the 5 prime
15 fragment being sequenced. On Slide 25, there are a couple of citations to
16 Linnarsson of the disclosure of the 5 prime fragment being sequenced.
17 That's not what they cite in their Petition.

18 So before moving on to Ground 2 and perhaps hitting on Petitioner's
19 new reply arguments, depending on time, I thought I would step through
20 Linnarsson's disclosures and how the Petitioner handled them in the Petition
21 particularly with respect to fragmentation and capture. And the disclosures
22 show Linnarsson's map A consistently uses fragmentation biotin and a
23 restriction enzyme cut site, so that's fragmentation and capture. And the
24 Petitioner treated them all as a single embodiment in the Petition and never
25 provided any obviousness argument to mix and match across them if they
26 are indeed separate embodiments. And these aspects of Linnarsson impact

1 the arguments involving sequencing limitation as well as ligation. So if we
2 turn to Slide 6, the method described in Linnarsson is called the STRT
3 method. The purpose is to generate a cDNA library which Linnarsson itself
4 defines as a collection of cloned complementary cDNA fragments. It's
5 undisputed that Linnarsson has only two examples, Examples 1 and 2. This
6 is clear from Linnarsson itself, and in deposition Dr. Cooper -- this is at
7 Exhibit 2020, page 94 lines 3 to 7, said he didn't remember any other
8 examples. If we turn to Slide 10, both of these examples, Examples 1 and 2
9 use the biotin related CDS, a TSO at the cut site, they add biotin to the CDO
10 -- excuse me to the TSO, bind the biotin ends to the beads, fragment, wash
11 those fragments away, and then cut using a restriction enzyme to free the 5
12 prime fragments. And if we turn to Slide 11 --

13 JUDGE FITZPATRICK: Ms. Raymond, I have a scientific question
14 here. When they're doing the biotin, do they -- I understand PCR is like a
15 very, you know, repetitive process. You do it a certain number of times.
16 Are they just adding biotin, like, the last time they do a PCR step? Or is it
17 always on the TSO?

18 MS. RAYMOND: So the -- there is sort of a big PCR step at the end
19 to amplify, but early on when we're doing this reverse transcription process,
20 the biotin, I mean, as it's described or pictured in Figure 11 for instance,
21 right, the biotin is already attached to the CDS and then there's biotin that's
22 added onto the TSO after the TSO is attached. And I think we see that
23 between steps, I believe it's C and D of Figure 11.

24 JUDGE FITZPATRICK: So did the biotin --

25 MS. RAYMOND: Between B and C you see that the TSO in B, the
26 yellow TSO if we look at Parse Slide 8 for example, and then in Slide -- in C

1 you see that the biotin has been added. Whereas the CDS is a little different.
2 The biotin is already on the CDS when the CDS sort of comes into play in
3 step A of Figure 11.

4 JUDGE FITZPATRICK: If you know the answer to this, please
5 answer it. Does the biotin -- I understand the argument that biotin would
6 interfere with the addition of a tag. Does the biotin if it's already on there,
7 does it interfere with PCR? With the polymerase chain reaction or is the
8 PCR already completely done by the time biotin is incorporated or added?

9 MS. RAYMOND: The biotin is the part of the PCR primer so -- I
10 apologize. I'm trying to , trying to fully understand your -- the question.
11 The primer --

12 JUDGE FITZPATRICK: It just keeps doubling, right. The strands
13 effectively just keep doubling, right, as you can -- on each step.

14 MS. RAYMOND: Oh. So you're asking whether as one is PCRing
15 the biotin disappears? Or, like, you know, the biotin isn't on additional
16 double stranded cDNA?

17 JUDGE FITZPATRICK: Well, I guess -- I mean, if the biotin is not
18 on -- it's get incorporated by the CDS or the TSO I'm not -- maybe both.
19 Does it then -- if the biotin is on any fragment of DNA, can you then do a
20 PCR amplification of it? Or do you have to remove the biotin?

21 MS. RAYMOND: I think you can do a PCR amplification of it. But
22 we have -- in Linnarsson there are a limited number of steps and a limited
23 number of really extension steps that we see between, you know, steps A
24 and C really. And then what we have going into Figure D of Figure 11 is the
25 internal -- there's this double-stranded DNA cut, and so the internal
26 fragments are washed away, right. And so what we see in Figure D and

1 Figure C is that on the two ends there's biotin. There's biotin on the two
2 ends of the cDNA that's fragmented, and then that biotin is what's required
3 to bind to the beads that we see in E. And that's why the internal fragments
4 of Figure 11 are washed away, because they don't have a biotin on them so
5 they can't bind to the bead. So what you end up with is, you know, at the
6 end of D or before you start doing this fragmentation is you have cDNAs of
7 biotin on both ends. You can cut and you know that you can still -- the two
8 ends you're able to stick to the beads because, you know, Figure E, those
9 ends stick to the beads and as Linnarsson says everything else is washed
10 away. Your Honor, I can't hear you. I don't know --

11 JUDGE FITZPATRICK: Yep. I was still on mute. Thank you, Ms.
12 Raymond. On Figures 3 and 4 in Linnarsson --

13 MS. RAYMOND: Yes.

14 JUDGE FITZPATRICK: -- the fragments that we're looking at, they
15 go all the way from a 5 prime to a 3 prime end, so they're presumably
16 complete fragments. There is no biotin there shown.

17 MS. RAYMOND: That's right.

18 JUDGE FITZPATRICK: Is that -- how do you -- I guess, how do
19 you account for that? They want -- they're emphasizing, hey, look at this.
20 There's no biotin here. Same deal with Figure 4. One of them I think is a
21 TSO, maybe one of them is a CDS. I can't remember. But why would that
22 be the case if Linnarsson always uses biotin?

23 MS. RAYMOND: Sure. The Figures 3 and 4 are showing a
24 polynucleotide sequence, and those Figures 3 and 4 are part of Example 1,
25 right. Example 1 uses biotin fragmentation that this whole process that
26 we've been talking about, about fragment and capture. And so if we look at

1 how they used -- they even themselves in the Petition use Figures 3 and 4,
2 what they use it for is to show that Figures 3 and 4 have a cell tag. And
3 what they use for their CDS over and over -- and they put a box -- they put a
4 green box around it and you can see this in Petition page 25 to 26 in their
5 Petition, page 41 to 42, and paragraph 110 of Cooper, is when they talk
6 about the CDS and the CDS that they're going to use, they have a green box
7 -- and we see Figure 11 green box around the Poly-T, the primer, and the
8 biotin, green box. And then, in fact, in Petition on 41 to 42, it then goes on
9 to talk about Figure 4 and says -- refers to the CDS, the CDS being the CDS
10 that they're talking about in Figure 11 and, frankly, Figure 2. And so that I
11 have mapped -- in their Petition they map these all as the same embodiment.
12 They have not shown any --

13 JUDGE FITZPATRICK: So let me -- let me -- I understand that
14 argument. It's been made. And you're at your time, so we're going to -- I'm
15 going to let you answer a question and you can still have your five minutes.
16 I understand that you're saying they treat everything as one. But why does
17 Linnarsson -- yeah, Figure 3 in Linnarsson doesn't have biotin in it. Will
18 you concede that?

19 MS. RAYMOND: I concede that it doesn't show -- it doesn't show
20 biotin on it.

21 JUDGE FITZPATRICK: Gotcha. Now, and same with Figure 4?

22 MS. RAYMOND: Correct.

23 JUDGE FITZPATRICK: Now, why wouldn't Linnarsson have
24 shown -- why would Figure 3 and Figure 4 be the way they are if Linnarsson
25 required biotin? Not the Petitioner. I understand Petitioner's ground, you're

1 saying that they require biotin. But why would Linnarsson have these
2 figures if -- if it requires biotin?

3 MS. RAYMOND: Because what Linnarsson --

4 JUDGE FITZPATRICK: Or is --

5 MS. RAYMOND: Sorry.

6 JUDGE FITZPATRICK: Or is it that Linnarsson doesn't require
7 biotin?

8 MS. RAYMOND: Linnarsson is showing the structure -- the
9 polynucleotide structure of the CDS. It's showing the ATS, it's showing the
10 cell tag, and it's showing, for instance, the Poly-T tail as structure of the
11 polynucleotides. Biotin is not a polynucleotide. Biotin is a different
12 chemical that's put onto the end. And so we see -- you know, we've seen in
13 Figure 2 there is a black box we see in Figure 11, of course, there's a bio. In
14 Figure 4 -- and I would say, I think, they cite Figure 3 and 4 as, you know,
15 comprising these pieces. I don't think there's in Linnarsson that tells us that
16 there's a reason why biotin would be shown there. It's presented again in
17 this context of Figure -- of Example 1, which uses the biotin. And what
18 they're trying to show by Figures 3 and 4 is that there is this structure of
19 polynucleotides where you have the APS, a primer, a cell tag in the middle
20 potentially -- because, of course, in some of the other figures they don't
21 show that that cell tag is in the CDS. So they're showing in the cell tag
22 where -- they're showing the CDS where you can find that cell tag and then
23 they're showing the, the part that actually anneals to the polynucleotide in
24 the process. So with respect to this CDS, that's this RCS that they show the
25 Poly-T that binds to the Poly-A tail of the mRNA.

1 JUDGE FITZPATRICK: Okay. Thank you for answering that
2 question. We'll keep your five minutes for rebuttal.

3 MS. RAYMOND: Thank you, Your Honor.

4 MR. WALTER: Your Honor, are you able to hear me all right?

5 JUDGE FITZPATRICK: Mr. Walter, yes.

6 MR. WALTER: Can you hear me okay?

7 JUDGE FITZPATRICK: You had reserved 15 minutes. We'll give
8 you 17 minutes. We'll keep it the same.

9 MR. WALTER: Okay. All right. You can hear me? I'm not sure
10 you can hear me?

11 JUDGE FITZPATRICK: Yes.

12 MR. WALTER: Okay. Great. Thank you.

13 JUDGE FITZPATRICK: If you can't hear me -- you can hear me?

14 MR. WALTER: I can hear you.

15 JUDGE FITZPATRICK: Great.

16 MR. WALTER: I can hear you. I just wasn't sure because I asked a
17 question a couple of times, and I didn't get an affirmative answer. So I had
18 to ask again. Sorry about that.

19 All right. I'm going to share my screen again. Are you able to see,
20 Your Honor?

21 JUDGE FITZPATRICK: Yes.

22 MR. WALTER: Okay. So one of the things I heard them state
23 during their presentation was that we asked Dr. Quackenbush a lot of unfair
24 questions and gotchas on things that were not in play. Here's one of the
25 things we asked him. Are you able to describe based on all your work in this
26 matter what you think is inventive about any of the claims in the '981

1 patent? Let's say someone wanted to know and asked you. Answer, I
2 haven't performed that analysis, so I'd be hesitant to render an opinion today
3 since it's outside the scope of my report. Now if there was anything that was
4 possibly in play in this case, it's this question. Because we're spending a lot
5 of time going through nitpicking on what's in our Petition, what's not in our
6 Petition, and all these arguments trying to contend that we missed concern
7 points in our Petition that we changed. My belief -- and I think that's been
8 borne out here today is that these kinds of arguments are stemming from the
9 fact that they're, they're just weak on the merits. Let's just take a step back
10 and look at what they haven't responded to. They haven't denied that dual
11 tagging was known in the art. They haven't denied the dual tagging was
12 conventional, that they admitted it in their previous case. They haven't
13 denied that ligation was a known conventional technique. They haven't
14 denied that a person of ordinary skill in the art, if they wanted to, could
15 increase the tag length to tag more polynucleotides if you needed to. They
16 haven't the challenged our motivation to combine. They haven't said that
17 that's wrong, that a person of skill in the art wouldn't be able to -- or
18 wouldn't be motivated to make the combination. They haven't challenged
19 reasonable expectations of success. When it comes to secondary
20 considerations, they put no evidence in. They just completely ignored that
21 aspect of the Graham factors. When it comes to all their flat out admissions
22 from the Becton and Dickinson case where they've admitted everything was
23 known and conventional, they haven't challenged any of that. When it
24 comes to the written description, they stood up at the beginning and said,
25 well, everybody knows you can have two inventions in a patent. Well, let's
26 look at what the patent says. Let's see if the patent characterizes tagging as

1 the invention. Let's see what the patent says. The patent doesn't say this is
2 the invention. The patent says this is something we previously did. The
3 patent says this is the prior art. The specification doesn't describe two things
4 in the invention. It tells you that the thing that they've claimed is the
5 invention is the prior art. Okay, so let's -- I just want to do a reset on all the
6 fundamental aspects of obviousness they've failed to address. I'm going to
7 get into the arguments they've made, and I'm going to try to respond and try
8 to address what I feel are the key points.

9 One of the things we heard them say when it comes to sequencing the
10 tagged polynucleotides is that Dr. Quackenbush, he got into it, and he started
11 diving in and what he understood Dr. Cooper to be saying was that you have
12 to sequence the entire plurality of the tagged polynucleotides. You have to
13 sequence the entirety. That's a -- I heard Ms. Raymond say, that's not what
14 Dr. Quackenbush understood when we asked him about it as his deposition.
15 He ostensibly presumably had looked at this stuff and his opinion wasn't,
16 yeah. I looked at Dr. Cooper's opinion and he clearly is relying on
17 sequencing the entire tagged polynucleotides. He says Dr. Cooper hasn't
18 offered any opinions on this point. He said it multiple times. So this notion
19 that the theory was somehow based on sequencing the entirety of the tagged
20 polynucleotides, that's just not there. That a late shift that they've moved to
21 -- to try to explain the fact that they had to change the kind of stealth claim
22 construction opinion that they offered.

23 And to answer your question, are they offering a claim construction in
24 the district court? No. What happening is that they're submitting expert
25 testimony where they're disavowing any suggestion that the claims would
26 require sequencing the entirety of the tagged polynucleotides. They're doing

1 that because I think they realize it would harm them what it comes to
2 infringement.

3 So I want to talk now about the questions of ligation. Your Honor
4 asked me a question during my presentation about how the ligation approach
5 would work, and I wanted to make sure that I address that. And so what I'm
6 showing now is Exhibit 1002. This is, this is Dr. Cooper's declaration
7 submitted in support of the Petition. And if you go over here to Ground 2,
8 this is where he lays it out. And as he explains here in paragraph 237, Dr.
9 Cooper explains, it would have been an obvious and routine design choice
10 with a reasonable expectation of success to carry out our modification by
11 ligating an oligonucleotide comprising the second tag sequence to
12 Linnarsson's CDS and/or TSO. So I want to do give you that cite, so you
13 can see real clear what the approach is here. You have no Linnarsson tag
14 which has the cell tag, and then you're ligating the -- you're ligating the
15 second tag sequence to that, and that's what Dr. Cooper's laid out. And one
16 of the things -- I got to just take a step back. There's been never any
17 challenge that the ligation wouldn't be routine or conventional. There hasn't
18 really been any challenge to whether a person of ordinary skill in the art
19 would be motivated to do this or have a reasonable expectation of success.
20 All the kind of fundamental issues related to obviousness they've tried to
21 push aside, and they haven't taken it on. But I wanted to make sure you had
22 that cite, so you're aware of where that was.

23 JUDGE FITZPATRICK: Mr. Walter, it's still -- there's still an issue
24 of it's a little bit of a -- doesn't perfectly fit, and that is, in the -- the Claim 1,
25 modification you're conceptually dividing the existing Linnarsson label into
26 -- to function as two tags.

1 MR. WALTER: Right.

2 JUDGE FITZPATRICK: All right. And then here in paragraph 237
3 that highlighted sentence, it would have been an obvious and routine design
4 choice with the reasonable expectation of success to carry out this
5 modification -- the one that you just referred to do I think, right?

6 MR. WALTER: Yeah.

7 JUDGE FITZPATRICK: Ligating an oligonucleotide comprising a
8 second tag sequence.

9 MR. WALTER: Yes.

10 JUDGE FITZPATRICK: But the modification was a conceptual one.
11 I'm not saying that this screws up your case, but can you -- so what would
12 the tag look like for Claim 5 for your modification? Would it be longer
13 then?

14 MR. WALTER: Okay. So let me try to --

15 JUDGE FITZPATRICK: The label. The full label. You know.

16 MR. WALTER: I think there's two questions embedded in there.
17 First, what is the modification? The way I've always thought about the
18 modification is that Linnarsson, it has one type of tag. It has the cell tag,
19 okay. And so the modification is you have to get the second tag. You have
20 to introduce the second tag to Linnarsson how, and you can do it multiple
21 different ways. One way, the way we've emphasized in connection with
22 Ground 1, is that Linnarsson talks about the cell tag being 4 to 20
23 nucleotides. Well, you can just divide it up, okay. That's one way you can
24 do it. And the other way -- really the only way, and this is what Dr. Cooper
25 explained in his declaration, is the other way you can make the modification
26 which is introduce a cell tag, is to ligate on an additional sequence to act as

1 your molecular barcode. And the way the tag would look is it would look a
2 little different from what's in McCloskey, which is that it's a randomer. And
3 you'd use a randomer because what's going to happen is you're going
4 introduce a pool of random sequences just like what McCloskey does, and
5 the random sequences are going to attach randomly to the molecules, and
6 because they attach randomly they're going to be able to uniquely identify
7 the molecule. And that's what McCloskey does. It uses a randomer. And so
8 you would just ligate a randomer. And what would the length be? Well, the
9 person of ordinary skill in the art following McCloskey would be able to
10 choose the length. McCloskey tells you how long it needs to be.
11 McCloskey tells you that the number of polynucleotides you can distinguish
12 is 4^N where N is the number of polynucleotides in your tag. So that's
13 what it would look like.

14 So continuing on with this numerosity issue -- this is their Slide 35.
15 And, you know, as I sat through the oral argument, you know, what was
16 interesting was Your Honor asked them many times where did they say that
17 their theory was reliant on tagging all the polynucleotides in a cell? And
18 they kept pointing Your Honor to examples where we talked about tagging
19 the polynucleotides in the sample. And that's important because the sample
20 doesn't require all the polynucleotides in the cell. They admitted that during
21 their presentation. They admitted in the district court. It doesn't require all
22 the polynucleotides in the cell. And so where they tried to kind of run to is
23 this little quotation right here. Linnarsson describes a method which is
24 designed to be applied to substantially all mRNA molecules of a given cell.
25 Okay. Now there is two things. First, this is not even part of this case. This
26 is another case. So they can't possibly come in here saying the Petition was

1 premised on this because their relying on something from another case.
2 Second, this passage they're talking about -- all it's saying that if you did
3 want to tag all the of the poly -- if you did want to tag all the mRNA
4 molecules in a cell, you could do it because Linnarsson is indiscriminate in
5 terms of the number of polynucleotides that is releasing. It's not saying that
6 the Petition is premised on that. It's saying that there's a dependent claim
7 that would be rendered obvious in view of Linnarsson. Now, let's look at
8 something else too. Let's say -- let's just assume arguendo that, you know,
9 you're talking about having to tag all the polynucleotides in a given cell.
10 Well, they kind of ramped it all up by saying it's about a mammal. But it's
11 not limited to mammalian cells. We asked Dr. Quackenbush on Slide 67,
12 are the '981 claims limited to mammalian cells? I haven't performed such
13 an analysis. This is just more dodging the testimony just at a 50,000 foot
14 level. All the dodging the testimony and complaining that this is an unfair
15 question. This is not an unfair question. Not for a Harvard professor who's
16 been an expert in 30 patent cases. This is a fair question, and this is just a
17 dodged answer because he doesn't have a good answer.

18 Even if you say that you have to do all the molecules in a cell,
19 Linnarsson tells you it doesn't need to be a mammalian cell. It can be a
20 prokaryotic cell. That's a bacterial cell. These are the simplest cells known
21 to mankind. I asked Dr. Quackenbush again, do you have to do it with a
22 mammalian cell? Well, he admits you can do it with yeast. Here's our
23 expert, Dr. Cooper. Bacteria such as E. coli have a little over 4,000 genes
24 and 1,300 mRNA molecules. And there's other types of that even less, 182
25 genes. Linnarsson tells you, you can do it with these kinds of cells. So you
26 can tag everything with seven nucleotides even if you wanted to. Dr.

1 Cooper gave an example had how you might use seven nucleotides. He
2 doesn't have to come in and say, okay. For a bacteria you do six. For a
3 yeast you do 20. For a mammalian cell you'd use 25. For a plant cell you'd
4 use 40. And then there's this funny kind of fish swimming out in the sea
5 that's got a massive genome and you need 50 for that. He doesn't have to do
6 that. A person of a skill -- of an ordinary skill in the art would know that
7 you have to change the length. A person of ordinary skill is not an
8 automaton, okay. And this is a fair response to a meritless argument on this
9 point. Now, it's all conventional. They've admitted that.

10 Let me make one more point. You know to try to respond to this --
11 and this just kind of gives you a good illustration of what their response is all
12 about, okay. What the lack of substance is underlying their response. When
13 we show them, hey, look., you don't have to do this on a mammalian cell
14 you can do this on a bacteria. Linnarsson says it. They're response was to
15 say, oh, well, bacteria don't have Poly-A tails. And they cited this testimony
16 from Dr. Cooper where they say, hey, look. Dr. Cooper admitted you can't
17 even use Linnarsson with bacteria because it doesn't have a Poly-A tail.
18 Well, their own evidence that they cite here on the bottom it says it does. It
19 says that you have RNAs with Poly-A tails when they're bound or
20 degradation. So they do have it. Linnarsson tells you can use it with
21 bacteria. But then here's what Dr. Cooper actually said during his
22 deposition. He said, I think there are evidence of polyadenylation in
23 prokaryotic organisms. Actually, I think it's there. My understanding is that
24 some bacteria have Poly-A tailed mRNAs at their ends. That's on Slides 74
25 and 75. And, in fact, one of the things he was asked about during his
26 deposition was a literature that talks about polyadenylation of mRNA in

1 prokaryotes. This was something that came up on page 136 and 140 of his
2 deposition. It was multiple literature articles. This is Exhibit 2104. This is
3 Exhibit 2105, RNA Polyadenylation in Prokaryotes. On the right,
4 Polyadenylation is an important post-transcriptional modification of
5 prokaryotic, eukaryotic, and organellar RNA. So it's there. And what has
6 been their approach in this case? Their approach in this case has been to
7 come in, take bits and pieces of Dr. Cooper's testimony out of context, and
8 say that people of skill in the art think there's no Poly-A tails in bacteria.
9 And then when we try to call them for taking this testimony out of context
10 and basing their position on something that's just incorrect as a matter of
11 science, they criticize us for trying to put things back in context, and contend
12 that we're introducing new arguments that shouldn't be considered on reply.
13 That's been their approach in this case. I don't think that's reasonable at all.

14 Now, another thing that we didn't get any response on was, hey, you
15 know, let's assume that Figure 11 is the only embodiment, which is wrong.
16 As Your Honor noted Figure 3 and Figure 4 --

17 JUDGE FITZPATRICK: Mr. Walter, just wanted to let you know
18 you have one minute.

19 MR. WALTER: Okay. They do not have a biotin. But let's just
20 assume that it's there, there's been no dispute that a person of ordinary skill
21 in the art would be able to make the modifications and make this work.
22 There's this biotin. They say that biotin gets in the way. Okay. The biotin's
23 in the way? Well, you know, look if you really want to use the biotin, put it
24 over here. Okay. A person of ordinary skill in the art would be able to make
25 that modification. Dr. Cooper opined to this effect in his declaration. You
26 can see that here. Maybe not here. But Dr. Cooper does have -- here it is.

1 It's on Slides 129 and 130 of our presentation. You can see Dr. Cooper
2 opines, hey, you can make the modifications. People are not unintelligent.
3 If you need to move the biotin around or move something around to make it
4 work, that's not going to be a problem. People know how to do that. They
5 didn't cross-examination -- cross-examine on this. Why not? Because they
6 know that's true. There's no answer to it, and they haven't disputed it here in
7 their presentation. So unless you have any questions, you've let me know
8 I'm out of time, I'm ready to let them do their five minutes of reply, and then
9 we can all go have lunch.

10 JUDGE FITZPATRICK: Thanks, Mr. Walter. I don't have any
11 questions, and the panel -- the panel does not either. So go ahead and
12 proceed.

13 MR. BAUGHMAN: Sorry. Didn't mean to interrupt. On mammalian
14 cells, this isn't something we made up, Your Honor. I call the Board's
15 attention to surreply pages 2 to 3 where we quote all the places that they
16 mapped to Linnarsson's Figure 1 tissue of interest to Figures 2 and 4 -- 2, 3,
17 4, and 11, and Examples 1 and 2 which analyzed eukaryotic mouse cells,
18 tissues, mouse cell types. If they thought it wouldn't work for those they
19 should have dealt with that in their Petition. Dr. Cooper admitted that most
20 bacteria do not have Poly-A tails. That testimony is on our slide. And as for
21 the citation to --

22 JUDGE FITZPATRICK: On the --

23 MR. BAUGHMAN: Yes, Your Honor.

24 JUDGE FITZPATRICK: On the issue of -- does it -- Linnarsson says
25 they use this for prokaryotic -- for prokaryotes. Doesn't it -- doesn't it say
26 that? Which would include bacteria?

1 MR. BAUGHMAN: Your Honor, there's no testimony about doing
2 anything in their argued combination with anything but a Poly-A tail. So --

3 JUDGE FITZPATRICK: I understand the argument about what their
4 Petition -- what position Petitioner took. I'm asking just about Linnarsson
5 itself.

6 MR. BAUGHMAN: Is it does mention that, Your Honor.

7 JUDGE FITZPATRICK: Because this portion is science because
8 you're making a scientific argument about the polyadenylate tails --
9 polyadenylated tails. But Linnarsson, I think, explicitly says they do this
10 with prokaryotes.

11 MR. BAUGHMAN: It does mention prokaryotes, Your Honor. But,
12 but they're only mapping it. It's a distinction Your Honor just drew. As we
13 show on Slide 41, they're only mapping is to using CDS's Poly-A tail. And
14 Dr. Cooper on the quotation, page 72 to 75, admitted that only a small
15 percentage of the transcripts with any given bacteria have such a tail. I'm
16 just responding to what Mr. Walter just argued. And then the only other
17 point I wanted to add unless Your Honor has questions on these is, I think I
18 heard mention of 182 mRNA in the bacteria, that's nowhere in their brief. It
19 is in paragraph 87 of Dr. Cooper. But by his own testimony, if you need ten
20 times as many, you have to have 18,200, again that fails with seven
21 polynucleotides, which is the only thing they mapped in their Petition. And
22 with that I will pass the podium. I know Ms. Raymond has a few things to
23 address unless you have a question.

24 JUDGE FITZPATRICK: No. Please proceed.

25 MS. RAYMOND: Thank you, Your Honor. Quickly, Petitioner's
26 Slide 47 and 48, they talk about Dr. Quackenbush not having an opinion.

1 And just to point out that the question really that was pending on page --
2 excuse me, Slide 47 was, is that a claim instruction issue evaluated? So
3 what he said is, I don't believe Dr. Cooper has offered any opinion, so I
4 haven't done that analysis. Again, I would just point you to the context of
5 that. And the testimony on Slide 48 is immediately after that same
6 testimony from Slide 47.

7 With respect to Ground 2, you know, there's this question, what is
8 their theory? What was their theory? You know, there are lots of reasons
9 that ligation doesn't work with Linnarsson. That's laid out in our briefing.
10 But, you know, generally their shortcomings of their ligation theory and
11 their failure to clearly point out its combination, I think, is what has gotten to
12 a -- gotten to some of this confusion in the first place. The Petition failed to
13 make clear about what was being modified. Linnarsson or the Ground 1
14 Linnarsson McCloskey combination, whether tags would be removed or just
15 added, wow many tags we added, when those tags would be added, and how
16 those tags would be added, and so forth. And on reply, we actually have a
17 slew of new arguments including even where the tag would be ligated. And
18 they say they'll ligate it to, you know, an extension product, not to the CDS
19 or TSO itself.

20 And then finally, with respect to their arguments now in rebuttal about
21 ligation and biotin and making modifications, I just note that, you know,
22 they're again, now adding more complications, more steps, and they've
23 never argued reasonable expectation of success even if you add and you
24 ligate to the CDS, which would have remain bound to the bead and isn't
25 sequenced. The sequencing disclosures we have are --

1 JUDGE FITZPATRICK: Ms. Raymond, can you -- I know you're
2 running out of time, but -- you just did -- but still answer this question. Can
3 you repeat that last point about what would remain bound and why?

4 MS. RAYMOND: Sure. So the CDS that's relied on throughout their
5 Petition is the CDS that ends up remaining -- remains bound to the bead. So
6 if we look at Figure 11, for instance, that bead binding, there's then -- there's
7 the restriction enzyme cut site that that's used that's, on the TSO side.
8 There's no -- they haven't relied on the restriction enzyme on the CDS side.
9 And in order to ever sequence the portion near the CDS, you would need a
10 restriction enzyme to cut the polynucleotide off the bead. And so what you
11 see -- again, when we're talking about the 5 prime end is sequenced and the
12 3 prime end is not sequenced, what we're saying is basically this TSO end
13 there's disclosure of sequencing that end, there's not disclosure of
14 sequencing the CDS end. So if you added the tag to the CDS end, it's never
15 going to be released from the bead and so it's -- there's no disclosure of
16 sequencing that.

17 JUDGE FITZPATRICK: Okay. I think we're done.

18 MS. RAYMOND: Sorry. They never argued reasonable expectation
19 of success for the whole thing if you then make that modification.

20 JUDGE FITZPATRICK: Thank you, counselor. We're going to --

21 MR. WALTER: Your Honor?

22 JUDGE FITZPATRICK: -- complete this, except we're going to open
23 this up to questions for any judges, if there's -- if there are any.

24 MR. WALTER: Your Honor, can you hear me?

25 JUDGE FITZPATRICK: Yes.

1 MR. WALTER: Would it be possible for me to respond for twenty
2 seconds of that last point?

3 JUDGE FITZPATRICK: No. We're good. We're looking at the
4 record. But I do want everybody to stay on here. We don't have any further
5 questions. We can go off the record.

6 (Whereupon, the proceedings at 3:13 p.m. were concluded.)

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