

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ALAMAR BIOSCIENCES, INC.,
Petitioner,

v.

OLINK PROTEOMICS AB,
Patent Owner.

Case IPR2024-01353
Patent 7,883,848 B2

Record of Oral Hearing
Held: December 9, 2025

Before: SUSAN L.C. MITCHELL, TAWEN CHANG, and
TIMOTHY G. MAJORS, *Administrative Patent Judges*.

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The above-entitled matter came on for hearing Tuesday, December 9, 2025, commencing at 12:57 p.m. EST, at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

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

12:57 p.m.

JUDGE MITCHELL: Good afternoon everyone. This is the final hearing in IPR2024-01353. The patent at issue is U.S. Patent Number 7,883,848 B2. The Petitioner is Alamar Biosciences, Inc. and Patent Owner is Olink Proteomics AB. I hope I said that right.

This hearing is open to the public. We do have a public line. And a full transcript of this hearing will be made a part of the record in due course.

I'm Judge Mitchell. And with me remotely are Judges Chang and Majors.

So, Counsel for Petitioner, would you like to identify yourselves and any of your colleagues?

MR. PLATT: Thank you, Your Honor. Christian Platt of Jones Day on behalf of the Petitioner Alamar Biosciences. Also with me today is Jennifer Bennett and Jesse Wynn.

JUDGE MITCHELL: And Counsel for Patent Owner, would you identify yourself and your colleagues?

MR. HOLMAN: Thank you, Your Honor. David Holman from Sterne, Kessler, Goldstein & Fox on behalf of Patent Owner Olink Proteomics. With me here today is Adil Moghal, also from Sterne Kessler.

JUDGE MITCHELL: Great. Thank you. Welcome to all of you.

Just a few housekeeping matters before we get started. We know there's a pending motion to exclude, and we will not rule on that today, but in due course with the final written decision.

You are certainly welcome, but not required to talk about any of the motions that are pending. There's also a pending motion to seal. But is it --

1 we think there is not going to be confidential information discussed today
2 during the hearing, but I wanted to confirm that affirmatively.

3 MR. PLATT: That's correct Your Honor.

4 JUDGE MITCHELL: Okay. And --

5 MR. HOLMAN: That's also correct.

6 JUDGE MITCHELL: Great. Thank you. So as set forth in our order,
7 and setting forth oral argument -- setting our argument, each side has 60
8 minutes to present its case. And we are -- will keep track of time for you
9 here. So certainly, when you get up to speak, and I know you all will,
10 identify yourselves and which party, and then certainly hold any objections
11 you have to anything that the other party has to say until your time to speak.

12 So very important for the record, and we love this, when you're
13 talking about a demonstrative, please identify the slide number that you're
14 talking about. If you're talking about exhibits, certainly also do so. Because
15 it's so helpful to go back in the record and be able to make sure we know
16 what you're talking about and what was said. So that would be very helpful.

17 So let me ask, first Counsel for Petitioner, would you like to reserve
18 any time for rebuttal?

19 MR. PLATT: Yes. Petitioner would reserve 20 minutes.

20 JUDGE MITCHELL: Okay. And, Patent Owner, you have the last
21 word for the day. Would you like to reserve time?

22 MR. HOLMAN: Yes, Your Honor. Patent Owner would like to
23 reserve 10 minutes for rebuttal.

24 JUDGE MITCHELL: Great. Are there any other issues that you need
25 to bring up before we begin that I missed?

26 MR. PLATT: Not from Petitioner.

1 MR. HOLMAN: Not from Patent Owner.

2 JUDGE MITCHELL: Thank you. All right.

3 As soon as I get the clock set, Petitioner we are ready to begin you
4 when ready.

5 MR. PLATT: So may it please the Board, so as we get started, if we
6 could pull up the '848 Patent. And this is going to be slide 4, and put up the
7 claim, Claim 1 there.

8 So the '848 Patent's reported invention relates to using nucleic acids to
9 bring together two molecules of interest to see if there's a functional
10 interaction between those molecules. It refers to that complex as a cis-
11 reactive cell.

12 Now the nucleic acids serve two functions. First, it has a
13 complementary region to allow for hybridization. That's what the patent
14 refers to as association elements.

15 Second, it has identification sequences, which are specific for each
16 molecule. So detecting those specific identification sequences allows for
17 detection of the functional interactions that occur.

18 If we could go to Slide 9. But this is not new, and the patent generally
19 acknowledged that it's not true well before the earliest priority date.
20 Matthew Kanan from Harvard published in Nature about current approaches
21 to what is called DNA templated synthesis. And that's Exhibit 1010.

22 Neri, another -- it's actually a published patent application, Exhibit
23 1011 described what's titled, Encoded Self-Assembly Chemical Libraries.
24 That describes molecules attached to nucleic acid sequences with common
25 hybridization regions on those two nucleic acids. What it calls Self-
26 Assembly Sequences.

1 Now the '848 Patent actually describes the Kanan and DTS approach.
2 And what the patent says is, in DTS two molecules are forced together by
3 using nucleic acids to allow the molecules to interact to a higher degree than
4 if they were not brought in proximity.

5 For example, and it says in Kanan, that's Exhibit 1010, one of the
6 molecules forced together is attached to a template nucleic acid which
7 specifically directs the second compound by direct hybridization of the
8 nucleic acid attached to the second molecule. And then it says, thus the
9 template nucleic acid contains both tags used to identify the compounds
10 which are forced together.

11 Now like the '848 Patent, Kanan further describes selecting what it calls
12 bond-forming combinations that occur between these molecules. And
13 identifying the specific template sequences corresponding to those
14 molecules in bond-forming combinations.

15 So if we could pull up Figure 1 from Exhibit 1010. And we're looking
16 at Figure 1A here. And as you can see, large pools of nucleic acids had to be
17 prepared. That's because if you look on the right, Pool B only has coding
18 region for its B1 molecule. But Pool A has both coding regions for A1, and
19 then B1. And then what happens is, for every Pool A molecule, you have to
20 have an A1 and a B1, and A1 and a B2, and A1 and a B3. And it goes on.

21 So making these pools was not easy. And Kanan's supplementary
22 information which is Exhibit 1013, was not before the Examiner. If we
23 could turn to Figure S1 from Kanan. And this is at page 3 of Exhibit 1013.

24 Now Kanan's supplementary information, it outlined the difficulties,
25 and number of steps involved in making these large pools. So making Pool

1 A members required six steps. And the B members at the bottom required
2 two steps.

3 Now the important part here is, that if you had to make 100 different
4 A substrates, and 100 different B substrates, for the different pool members
5 you would have to make 10,000 Pool A members, and you'd have to make
6 100 Pool B members. So a pretty significant amount of synthesis that has to
7 be done on the DNA in order to generate these different members.

8 But there were ways to decrease the size of these large pools that
9 needed to be created. So if we go back to Slide 9, that other reference was
10 the Neri reference, Exhibit 1011. And if we could pull up Figure 5 on page
11 6.

12 And Neri describes the use of these self-assembly sequences. And
13 what we can see in sublibrary A on the left has, DNA sequence designed to
14 hybridize to the DNA sequences of sublibrary B on the right.

15 Now the hybridization region on A is interrupted by a small segment
16 called the d-spacer. And then both oligonucleotides include a unique
17 sequence for each member of the sublibrary. You see that called Code A
18 and Code B.

19 Now those self-assembly sequences allow any member of Pool A to
20 hybridize with any member of Pool B. Further, as you can see on the right,
21 Neri provided for polymerization. And what that would do is, put Code A
22 and Code B on the same DNA fragment.

23 But the important part here about Neri is, in that earlier example
24 where we were talking about 100 substrates of A and 100 substrates of B, a
25 person of skill in the art using the Neri self-assembly sequences would only

1 have to make 100 Pool A members and 100 Pool B members. That's a 98
2 percent reduction in synthesis time.

3 So a person of skill in the art looking to adopt Kanan in order to save
4 time building these libraries would look to the Neri reference for better
5 sensitivity, and would have been motivated to use the self-assembly
6 sequences, and the polymerization of Neri with Kanan to achieve a more
7 efficient way of evaluating the functional interactions between molecules.

8 And if we could look at Slide 20, and if we zoom in on the right there.
9 And this is the figure reflecting sort of the cartoon of what the Pool A and
10 Pool B molecules would look like in the Kanan-Neri concept.

11 And you can see at the top there's the coding region for A, and then
12 there's the self-assembly sequence to B. And then the Pool B has a self-
13 assembly sequence to A. It's no longer specific to A1, B1, all that. But you
14 do have then, the specific identification sequences for each molecule that's
15 attached to the oligonucleotide.

16 This is what represents Ground 1, and Exhibit 1013 provides further
17 support for the motivation to combine. Now Ground 2, which we'll get to
18 later, adds a simple step of ligation as described in Famulok, Exhibit 1012,
19 and demonstrates the dependent claim 16 is also unpatentable.

20 So if we could turn to Slide 17. And looking at the elements of Claim
21 1, you would think that Patent Owner disputes only two limitations. That's
22 1D, and 1E. Patent Owner doesn't appear to dispute 1B, which relates to the
23 formation of CRC's, cis-reactive cells.

24 Instead, Patent Owner misreads the evidence provided under 1B,
25 including key discussion in the Petition regarding the polymerization
26 associated with Neri's self-assembly sequence which causes downstream

1 consequences in the analysis of limitations 1D, and 1E which they do
2 dispute.

3 Thus, in -- going through this analysis, we need to spend some time
4 discussing 1B. And as you can see, that relates to the formation of the cis-
5 reactive cells. Now --

6 JUDGE CHANG: Counsel, I just wanted to interrupt for a minute.
7 So in terms of element 1B, I just want to make sure. You talk about
8 polymerization. Is that basically, essentially the one embodiment that you're
9 arguing? Because I know there's also Claim 17 which does talk specifically
10 about polymerization.

11 But is that, basically is Petitioner limiting its arguments to the
12 embodiment where you had polymerization?

13 MR. PLATT: So Your Honor, when you look through the claims, and
14 the analysis that's done. Certainly when you get to step 1B, you look at
15 association. And we'll touch on this. There's two types of -- that we get
16 into. The first is just association of the nucleotides. The second part of it is
17 association via polymerization.

18 Now with respect to, when it continues on to the step D and E, it is
19 important to take into account the polymerization that takes place. Which as
20 you recognized, comes up in dependent Claim 17.

21 JUDGE CHANG: Okay. But I guess what I mean is, the
22 polymerization itself is not discussed in Claim 1. Other than I think you did
23 mention it in the reason to combine. But other than that, it's not discussed
24 specifically in the Claim 1 element. Is that right?

1 MR. PLATT: Well so Your Honor, with respect to -- I guess it
2 requires a little bit more -- it's more nuanced than that I would say. Because
3 Claim 17 is dependent, it's a dependent claim for them knowing Claim 1B.

4 You know, we know that if the dependent claim is found obvious,
5 then the independent claim by rule, is also obvious. And when we look at,
6 when we're doing the analysis of Ground 1, we discuss -- and let me, I think
7 it would be helpful to pull up -- if we could go to, let's go to Slide -- if we
8 could go to Slide --

9 Actually, let's pull up the petition, Jesse, pages 20 to 21.

10 And so before walking through the analysis of Claim 1, the Petition
11 does go through and explain that it would have been, that a person of skill in
12 the art would have been motivated to combine the polymerization of the
13 substrate pair that's disclosed in Neri with the method disclosed in Kanan
14 because the polymerization creates double-coating code on the extended
15 nucleic acid sequence to increase the specificity of the acid.

16 And that was supported by Dr. Nelson's declaration. If we go on to
17 page 23, the Petition again explains why a person of skill in the art would
18 reasonably expect success with the polymerization of oligonucleotides as
19 taught in Neri. It could have readily applied to oligonucleotides taught in
20 Kanan because the use of primers and polymerized enzymes to extend
21 oligonucleotides was a standard practice when the application was filed.

22 And then, as Your Honor noted, when we look at dependent Claim 17
23 -- but before we get to that, why don't we jump forward to the Petitioner 35
24 through 36.

25 And this is in the context of -- do you want to go to that Jesse? All
26 right.

1 And this is in the context of step 1E in Claim 1. And what the
2 Petition explained is that a person of skill in the art would have understood
3 Kanan in view of Neri, that the detection of the bond-forming substrates
4 product permits the detection of the at least two identification sequence
5 elements because it is the resulting nucleic acid which includes the two
6 identification sequence elements of Neri that is detected, and corresponds to
7 each unique substrate.

8 So what that's referring to is, I think we know it, as Patent Owner
9 pointed out, right, in the -- where you only have association without
10 polymerization, that disulfide bond cleaves one of those oligonucleotides.
11 But when we're looking at polymerization, you actually do have the two
12 sequence elements, or the two identification sequence elements that actually
13 then continue through to step E. And --

14 JUDGE CHANG: Okay. Thank you. So I think I understand. I just
15 want to make sure, so polymerization is necessary in order for the
16 Petitioner's case for step E. Is that correct? Polymerization is required.

17 MR. PLATT: That's right. Polymerization is used. And in the
18 polymerization, or association via polymerization. And that's what's
19 discussed in dependent Claim 17.

20 And if we go -- if we could go to dependent Claim 17, discussion of
21 the Petition on pages 33 to 34. And this is where we specifically address the
22 fact that Kanan in view in Neri discloses the limitation. It includes, in
23 example 3, that the oligonucleotides -- I won't read it here, but it does
24 explain how Neri discloses example 3 which can then be incorporated into
25 Kanan, that then adds that double coding.

1 And it goes on to say that a POSA would have understood that it
2 would have been obvious to use the polymerization of the oligonucleotides
3 as taught in Neri with the creation of the paired substrates in Kanan. So
4 that's an important consideration when you're looking at what the timing of it
5 is.

6 It is actually what occurs in step 1B of the patent on forming the cis-
7 reactive cells. And it's specifically at the time those substrate -- those paired
8 substrates are prepared in Kanan, that double coding occurs through
9 polymerization.

10 And if we look at Slide 59. And this is the dependent Claim 17. And
11 what I would say is two things on this which is, the Patent Owner's own
12 expert agrees that in terms of -- in terms of the polymerization that takes
13 place in the Kanan and Neri construct, that it would actually double code the
14 -- onto the other nucleic acid so that both identification sequences were
15 included there.

16 And he also agrees that this Claim 17, when it's talking about
17 association as via polymerization, that's the association that's discussed in
18 Step 1B of Claim 1.

19 And if we look at the disclosure, this is the example 3 of Neri that was
20 discussed on the specific polymerization method that would be used in the
21 Kanan and Neri combination.

22 Now you know, we talked a little bit about creating the CRCs, and the
23 process that's involved there. You know, Patent Owner's argument is based
24 on sort of ignoring what has taken place in that, in limitation 1B.

25 And so if we actually look to the next slide, and this is Patent Owner's
26 Slide 34. Okay. All right. We've got it on the screen.

1 So this is with respect to Patent Owner's Slide 34. And it says there, it
2 says the Petition does not explain if, when, or how a POSA would have
3 allegedly implemented a polymerization step.

4 And what I noted about this slide that I thought was particularly
5 interesting is, you note that it actually starts at Step C. It does not include
6 Steps A and Steps B. And that's precisely where this would have occurred.

7 And so when it says that we don't discuss, the Petition doesn't discuss
8 the if, that's wrong. The Petition demonstrated that a Person of Skill in the
9 Art would be motivated to do polymerization with a reasonable expectation
10 of success resulting in a nucleic acid with both codes. That's what ultimately
11 ends up in 1E that allows for the detection of each of the sequence
12 identification elements.

13 As for when, the Petition explained it would be during Step B's
14 association in the Claim 17 analysis, because it would be part of the
15 Kanan/Neri cis-reactive cell formation. As for when, the Petition explained
16 that it would be during Step B's association in the Claim 17 analysis within
17 limitation Step B, because it would be part of the Kanan/Neri CRC
18 formation.

19 And for how, the Petition explained that it was the use of primers and
20 polymerized enzymes to extend oligonucleotides that was standard practice
21 at the time of the invention.

22 So with that background on the creation of CRCs, let's look at what
23 the remaining steps are. And if we could pull up Exhibit 1010, Figure 1B
24 from Kanan. Okay. So this is Figure 1B from Kanan.

25 And looking at what takes place here, so there's various Pool A and
26 Pool B substrates that are all put in a solution, and a set of reaction

1 conditions is applied. Now that may result in bond formation between A
2 and B molecules.

3 And this results in two types of combinations. Non-bond-forming
4 combination somewhere on this top line here, that's shown sort of on the left
5 after the arrow. And bond-forming combinations which are shown on the
6 right, which shows that green bond between B9 and A6.

7 Now let's compare that with the Kanan and Neri combination. And if
8 we could go to Exhibit 1005, this is Dr. Nelson's declaration. And put up
9 pages 63 and 67 side by side.

10 And what we can see is that with respect to association, that's the -- on
11 the left-hand side is what is shown as those without having a functional
12 interaction because there is no bond between B9 and A6. And on the right-
13 hand side, where there is a functional interaction, where B9 and A6 has
14 bound to each other, that's shown by that green line. And the biotin that's
15 attached to B9 is what is ultimately the detectible trace.

16 Now --

17 JUDGE CHANG: Sorry, let me just ask. So this is Exhibit 1005, Dr.
18 Nelson's declaration. What page are you on?

19 MR. PLATT: This is pages 63 and 67.

20 JUDGE CHANG: Okay. Thank you.

21 MR. PLATT: And then, if we look at the visualization of association
22 via polymerization, and that's in Exhibit 1051, and this is Dr. Nelson's
23 second declaration at pages 17 and 18, putting those side by side.

24 And what we see there is then, on the left-hand side is the equivalent
25 of the non-bond-forming combinations. Again, now what we see is with the

1 polymerization identification sequences are on both -- on both the A strand
2 and the B strand. I'm sorry, on the A strand.

3 And on the right-hand side, you see it with a functional interaction.
4 Again, B9 is bound to A6 with that green line. And it shows that the
5 identification sequences are on the A strand.

6 JUDGE CHANG: So Counsel, I do have a question about this. And
7 this relates to something you discussed before, when the polymerization
8 takes place. So if you look at Figure -- sorry, the figure on page 17. So does
9 the polymerization occur before or after? I understood you said it's during
10 Step B, but before or after the disulfide cleavage?

11 MR. PLATT: It takes place before.

12 JUDGE CHANG: So it's before. If it's -- so as I understand it though,
13 the association element is the same for all A Pool -- Pool A molecules, and
14 all Pool B molecules. And therefore, the idea is that every single Pool A
15 molecule will bind to every single B Pool molecule.

16 MR. PLATT: That's right. It's combinatorial.

17 JUDGE CHANG: Right. And so if you haven't cleaved the disulfide
18 bond, then when you are doing a polymerization aren't you getting,
19 essentially every single B identification, B Pool identification tag? Because
20 they're all associated.

21 MR. PLATT: That's correct, Your Honor. And the -- that's the reason
22 why it's done before selection. Because if you go through and do that, the
23 disulfide bond selection process that takes place in Kanan, if you wait to it
24 until after, it's not going to work.

25 The other thing is, when you're looking at it ahead of time before that
26 cleavage takes place, if you don't do that cleavage then what you're going to

1 end up having is, you're going to end up having all of the non-bond-forming
2 combinations, those without a functional interaction, those will bind in the
3 streptavidin, or you're going to have -- and you will have those that do have
4 functional interactions binding to the streptavidin.

5 So that then when you do the DNA sequence analysis, you're not
6 going to be able to tell which ones have that functional interaction or not.

7 JUDGE CHANG: Well I guess my confusion comes from the fact
8 that I think all Pool B molecules will have the biotin that will bind to the
9 streptavidin regardless of whether they form the functional interaction.
10 Right?

11 So let's say, if you're looking at the non-bond-forming combination
12 here on page 17, it's down to -- isn't it still down to the avidin, or is it not
13 bound at that point?

14 MR. PLATT: So what happens is, it's because of the disulfide
15 cleavage process. So I think you know, one of the ways to look at it, I don't
16 know if you can see it or not, I've got a highlighter and a pen. Right? Is you
17 have -- assume this is, you know, the ends are the molecules of interest.
18 Right?

19 And what's happened is, when you have the non-bond-forming
20 combinations. So again, these are just annealed together. Right? And you
21 have that disulfide bond cleavage that comes in. That molecule with the
22 biotin attached, right, will still be in there. But both of these other two
23 sequences are going to float away leaving only the molecule of interest with
24 the biotin attached, or the B.

25 Here in this case it would be B9 assuming it was not involved in a
26 functional interaction. But it has no nucleic acid sequence attached to it.

1 So, and the difference there is when you have a functional interaction,
2 and again now they're connected together at the ends of the molecules of
3 interest. When that disulfide bond cleavage occurs what happens is, now
4 the, ultimately the B strand goes away, but the A strand, with its double
5 coding on it, is still in the solution. And then that is what binds to the
6 streptavidin, and then you can detect the sequences that exist there. And
7 that's why --

8 JUDGE CHANG: Yeah. Sorry. I guess my confusion is, if you're
9 doing the polymerization before the disulfide bond, don't you still have the B
10 molecules that's non-functional interacting with the A molecule? Isn't that B
11 molecule, isn't that polymerization going to happen as well? How are you
12 distinguishing between the polymerization -- how are you able -- before the
13 disulfide cleavage, how are you able to distinguish the polymerization to
14 only those that have the formational bond between A and B? I guess that's
15 my question.

16 MR. PLATT: So I think as we can tell on the left-hand side here, and
17 the right-hand side. So these would both be in solution. Right? You would
18 have both the non-bond-forming would be polymerized as well as the bond-
19 forming combinations as well.

20 So the part that is actually doing, and this is the selection. Right? The
21 part that is doing the selection is that disulfide bond cleavage which then
22 allows for you to separate out, right, those that have the functional
23 interaction from you know, everything else that didn't.

24 JUDGE CHANG: Right. So I guess, maybe I'm not making myself
25 clear. So if you -- so if you are, you do separate it out once you have the
26 disulfide bond cleavage. But isn't the nucleic acid moiety that's left, that has

1 the polymerization added, doesn't it also have the B identification sequence
2 of the non-functional?

3 I understand that the B, you know, the sequence from the B molecule
4 has floated away. But the A molecule nucleic acid which remains, that
5 already has the coding for the B that's non-functional interacting because
6 you've done the polymerization before the cleavage. Is that --

7 MR. PLATT: So --

8 JUDGE CHANG: What am I missing there?

9 MR. PLATT: So that's correct, Your Honor. And this is part of the,
10 the clever part if you will, of Kanan. Which is the biotin is only attached to
11 the B molecule.

12 The biotin is not attached to the A molecule. It's that functional
13 interaction that connects the B and the A such that when again, when the
14 streptavidin attaches to the biotin, it's only going to be attaching -- it's going
15 to go streptavidin to biotin to B and to A where there's a functional
16 interaction. That's what's shown on the right with that green line.

17 But on the left, when there is no green line, and that disulfide bond
18 has been cleaved, the A strand will wash away. And the B molecule,
19 because of the disulfide bond cleavage, will no longer be attached to the
20 nucleic acid. So --

21 JUDGE CHANG: Well I guess, let me ask this another way. So once
22 you have done -- you do the polymerization. The disulfide bond is there.
23 You do the polymerization. Now you attach it to avidin, and you cleave the
24 disulfide bond. What is left after the polymerization, after the disulfide
25 cleavage? What is left?

1 What tag is left on the nucleic acid molecule in A6? Do you have the
2 identification sequence of A? Does it have both? And if it does have both,
3 which I understand is what Petitioner is arguing, how do you know that
4 identification sequence for element B is only on the ones that have
5 functionally interacted?

6 MR. PLATT: Okay. So --

7 JUDGE CHANG: Does that make sense? More sense? Okay.

8 MR. PLATT: I think so, Your Honor. And I apologize if I'm not
9 being clear on it.

10 But I thought it might be helpful to go back and look at Figure 1 again
11 of Kanan, and looking at what's happening with this disulfide bond cleavage.
12 And what you can see is that on the top, again the biotin is only attached to
13 the B3. Right? And on the right-hand side we have B9 bound with A6.
14 That's what we call a functional interaction.

15 And when that disulfide cleavage occurs, you can see the non-bond-
16 forming combinations, that's A12. Those float away. Now yes, they're still
17 in solution of B3 bound to biotin, but it has no nucleic acid associated with it
18 due to the disulfide bond cleavage.

19 What's left then is, the B9 to A6 that's connected to biotin that then
20 binds with the avidin as shown here which allows for the selection of, what
21 it refers to as the bond-forming combinations.

22 And I note there that, you see the bond-forming is the spot -- the piece
23 between B9 and A6. The combination is the nucleic acids that are annealed
24 together. And what you're selecting for is, the only way that you're going to
25 know that you have this bond forming combination, and be able to identify it

1 and do the analysis that Claim 1 is all about in terms of detecting this, is to
2 do that disulfide cleavage analysis to get everything out of there.

3 This is what ends up being bound. And then you can detect the
4 identification sequence elements.

5 JUDGE CHANG: Okay. Thank you. I know you have other
6 arguments to make, so I thank you, that's a good explanation.

7 MR. PLATT: Thank you. And let me see, we're running a little short
8 on time, and I do want to talk just briefly about Ground 2. And if we could
9 go to Slide 66.

10 And what that addresses is the Famulok reference that adds
11 associations as via ligation using a splint oligonucleotide. And again, the
12 Petition goes through and demonstrates that for Ground 3, that additional
13 limitation is not anything new.

14 And in the last note, we did want to touch on Grounds 3 and 4. And
15 Ms. Bennett was going to handle that argument, if that's okay with the
16 Board.

17 MS. BENNETT: May it please the Board, I'm Jennifer Bennett for
18 the Petitioner. And I will be very quickly addressing Ground 3.

19 So unlike Grounds 1 and 2, Grounds 3 and 4 are based on the
20 positions that Patent Owner is taking in co-pending district court litigation
21 that the '848 Patent reads on Petitioner's NULISA product that is based on
22 proximity ligation assay, or PLA.

23 So PLA is a known method to detect predefined targets through
24 known affinities. The '848 Patent itself identifies both Baez, which is
25 Exhibit 1003, and Landegren, which is Exhibit 1004 as describing PLA.
26 And these are the two references that are at issue in Ground 3.

1 So the key issues with respect to Ground 3 are, if I can please have
2 Slide 72 --

3 JUDGE CHANG: I'm sorry, let me just interrupt very quickly before
4 you get started.

5 MS. BENNETT: Sure.

6 JUDGE CHANG: So does Petitioner agree that if we use the
7 construction, the claim construction of the terms as an ordinary -- person of
8 ordinary skill in the art would understand it, do you agree that Ground 3 and
9 Ground 4, that Baez and Landegren will not invalidate the claim?

10 MS. BENNETT: We do, Your Honor. So our position with respect to
11 Grounds 3 and 4 rely expressly on the positions that Patent Owner has taken
12 in the district court litigation. And if a person of skill of ordinary art were
13 aware of the positions that Patent Owner took in Exhibit 1008 for example,
14 in its complaint, then one of ordinary skill in the art would view, only with
15 that assumption, then one of ordinary skill in the art would view Baez and
16 Landegren as relevant art.

17 JUDGE CHANG: Okay. Thank you.

18 MS. BENNETT: And so the key issues with respect to Ground 3 are,
19 first whether the Petition mapped the molecules of interest on the antibodies
20 in Baez. Because if so, Your Honors, there's actually no dispute that Baez
21 teaches Claim 1A since Patent Owner doesn't actually substantively dispute
22 that the antibodies in Baez are molecules of interest.

23 But the Petition and the declaration of Dr. Nelson do map Baez's
24 antibodies as the molecules of interest in the exact same way that the Patent
25 Owner mapped NULISA's antibodies as the molecules of interest. So there
26 actually should be no dispute with respect to Claim 1A.

1 Second, the issue regarding Claim 1D is whether Baez teaches
2 selecting CRCs, or only detects CRCs. But Baez teaches affinity
3 purification which is a form for selecting using a biotin linker that allows
4 isolation of the CRCs on a mobilized streptavidin.

5 This selecting only occurs with the CRCs in Baez that had the
6 functional interaction. And in Baez, Your Honors, it's ligation that is the
7 functional interaction.

8 JUDGE CHANG: I'm sorry. Let me just ask two quick questions.

9 MS. BENNETT: Sure.

10 JUDGE CHANG: One is, so I understand in the Petition I believe
11 there are places where Petitioner says the molecule of interest is the
12 conjugate. Meaning both the antibody and the nucleic acid. I understand the
13 Petitioner has taken the position that actually the molecule is the antibody
14 and not the nucleic acid per se.

15 So my question is one, it does seem like Petition has said that the
16 conjugate is the molecule of interest in its entirety. And the second is, as I
17 understand it the functional interaction that we're talking about is a ligation
18 which occurs at a nucleic acid moiety.

19 So if we're saying that an antibody is a molecule of interest, what is
20 the functional interaction that Petitioner's arguing is occurring between the
21 molecules of interest?

22 MS. BENNETT: Yes, Your Honor. So I'll start with your question
23 with respect to whether it is Petitioner's position that the molecule of interest
24 is the antibody conjugate.

1 So to be clear, it is Petitioner's position that the molecule of interest is
2 the antibody, and not the antibody conjugate. And the best example of this,
3 if I can have Slide 77 please.

4 And so Slide 77, this is taken from the declaration of Dr. Nelson in
5 support of the position -- petition. And this shows the mapping of NULISA
6 to the '848 Patent on the left, and then applies that same mapping on Baez
7 for Claim 1A on the right.

8 And as shown here on the slide, the antibodies are designated as green
9 and yellow. Those are identified as the molecules of interest in both Baez
10 and in Patent Owner's reading of NULISA in Exhibit 1008.

11 And then the figure goes on to show that in both Baez and Patent
12 Owner's claim charts that the nucleic acid moieties, Your Honor, those are
13 what are depicted in blue and red. And those are not part of the molecules of
14 interest.

15 Now Your Honor did mention that at one point in the petition, it is
16 true that molecules of interest were referred to as antibody conjugate. And
17 unfortunately that was language that was taken over from the complaint
18 against Petitioner in Exhibit 1007 at paragraph 22 where the Patent Owner
19 referred to the antibody -- the capture antibody and the detection antibody as
20 an antibody conjugate.

21 But when you look at a whole, Your Honors, I believe there are at
22 least five separate instances in both the Petition and the declaration of Dr.
23 Nelson where it is very clear that the Petition is applying Patent Owner's
24 position in Exhibit 1008. And that the molecules of interest are the
25 antibodies.

1 And the best evidence of that is, when you look at the discussion of
2 the dependent claims 5, 6, 7, and 8 of the Petition at pages 64 to 65, you can
3 see repeatedly Your Honors, that it is the molecules of interest. And then in
4 parentheses for example on the slide on the screen, which is taken from the
5 petition, that the molecules of interest that we're talking about is the
6 antibody, and not the antibody plus the nucleic acid moiety. Because that
7 would be the interactor or what's called the reporter conjugate in Baez.

8 And the Petition is quite clear that the interactors are the reporter
9 conjugates in Baez which are the antibodies plus the nucleic acid moiety.
10 And with that I see that my time is up.

11 Does the Board have any more questions?

12 JUDGE CHANG: Nothing else.

13 MS. BENNETT: Okay. Thank you so much.

14 JUDGE MITCHELL: Thank you. Whenever you're ready.

15 MR. HOLMAN: Thank you, Your Honors. May it please the Board,
16 David Holman for Patent Owner Olink -- excuse me -- Olink Proteomics.

17 What we just heard from Petitioner this afternoon is based on a
18 superficial view of the '848 Patent's claim methods and disclosures in
19 Petitioner's asserted art combinations.

20 Just as it did in the petition, Petitioner's argument today has glossed
21 over express language in '848 Patent's claims, and has expressed teachings in
22 its asserted art, all in hopes of getting the Board to overlook the petitioner's
23 failure to make its case in the Petition for institution.

24 Now since the Board's institution decision, we now have a developed
25 record that underscores several fatal flaws affecting all four of the

1 Petitioner's grounds for unpatentability. And we have these summarized on
2 Patent Owner's Slide 8.

3 As we've explained in our briefing, there's at least two major
4 fundamental problems with Petitioner's arguments here. The first is that the
5 Petition fails to show that its art combinations teach or suggest all of the
6 elements of the challenged claims.

7 In Grounds 1 and 2, Petitioner relies on the combination of the Kanan
8 and Neri references. And Petitioner fails to show that this art teaches or
9 suggests at least Claimed elements 1D and 1E, and separately also fails to
10 show that this art combination with the Famulok reference for Ground 2
11 teaches all the elements of Claim 16.

12 In Grounds 3 and 4, Petitioner fails to show that its art combination of
13 Baez and Landegren for Ground 3 teach or suggest all the claim elements of
14 1A, 1D, and 1E. So now this failure to show all the claim elements are
15 taught or suggested in a prior art is fatal across all four grounds.

16 All right, the Board can end its enquiry there. But there's more. All
17 right. So the second problem that the Petitioner has is that it's failed to
18 demonstrate that a person of ordinary skill in the art would have been
19 motivated to make these modifications to the art as presented in the Petition
20 with a reasonable expectation of success.

21 Additionally, as we've explained in our briefing, the Petitioner's
22 arguments here have been a moving target since the start of this trial because
23 Petitioner's improperly changed and pivoted its arguments in reply.

24 When the Patent Owner's response explained the severe design flaws
25 in Petitioner's proposed modifications of the art, Petitioner responded not by
26 explaining why the original Petition was correct, but instead pivoting to

1 different disclosures in the Kanan combination for example, and attempting
2 to backfill the conclusory explanations, and cure other defects in the petition.

3 But the statutes, legal precedent, and this Board's rules are clear. That
4 a Petitioner in an IPR is obligated to make its case in the Petition to institute.
5 And of course, Petitioner is who carries the burden here. The burden of
6 persuasion stays with the Petitioner throughout the entire trial.

7 Okay. So let's start, I'd like to start by addressing Ground 1,
8 combination of Kanan and Neri, and Claim 1D the selecting step. If you
9 could please turn to Patent Owner's Slide 10.

10 So this is just a snapshot of the language in Claim 1. And of course,
11 the method of Claim 1 cites five steps, A, B, C, D, and E. Step A recites
12 forming the plurality of interactors. Right? Step B recites forming the
13 plurality of cis-reactive cells from those interactors. Step C refers to
14 subjecting the cis-reactive cells to those conditions that simulate a desired
15 functional interaction having a detectible trace.

16 Step D is a selecting step, selecting all cis-reactive cells exhibiting the
17 detectible trace. And then of course, Step E refers to subjecting the
18 associated oligonucleotides from those cis-reactive cells that were selected
19 to an analysis.

20 Now while the Petitioner states that the claim terms are given their
21 plain and ordinary meaning for Grounds 1 and 2, that's on Petition page 12,
22 Petitioner's reply arguments depart from this express language of the claims.
23 And they focus on a single word, selecting. Rather than reading this claim
24 element 1D as a whole.

1 In other words, Petitioner ignores what must be selected in Claim 1D,
2 and that is a cis-reactive cell. So let's take a look at what is a cis-reactive
3 cell. What is required for a cis-reactive cell? If you turn to Slide 13 please.

4 Now there's no dispute between the parties that a cis-reactive cell of
5 the '848 Patent requires at least two interactors. That's clear from the
6 express language of the claim. You can look at Claim 1B on the top left
7 there which recites, a cis-reactive cell comprises at least two interactors.

8 It's clear from the definition in the specification, which is on the
9 bottom left there. And I'll note that the Board you know, agreed that this
10 definition in the specification appears to be consistent with the plain and
11 ordinary meaning of a cis-reactive cell as it would have been understood by
12 a person of ordinary skill in the art, in view of the claims, the specification,
13 and the prosecution history of record. That's the decision on institution,
14 page 13, footnote 9.

15 And as I mentioned, there's no real dispute here on the definition of a
16 cis-reactive cell. Dr. Nelson -- you can see from Dr. Nelson's testimony in
17 his deposition there on the top right. There are statements in his declaration
18 or figures which you can see at the bottom. The bottom right here, that the
19 cis-reactive cell requires at least two interactors.

20 Well, so what's an interactor? Okay. That's on the next slide, Patent
21 Owner's Slide 14. Again, there's no dispute that an interactor of the '848
22 Patent is a molecule of interest coupled with at least one nucleic acid moiety.

23 You can see that from the express language of the claim in the top left
24 there. You can see that in the definition in the specification. That's at
25 column 9, lines 33 to 34. And again, the Board noted that this definition of

1 an interactor is consistent with the plain and ordinary meaning of that term.
2 Again that's --

3 JUDGE CHANG: Let me -- sorry, Mr. Holman, let me ask a
4 question. I just want to just clear up something I'm wondering about.

5 So I don't necessarily think that there's dispute about what the cis-
6 reactive cells or the interactors are. But isn't it -- I mean, I think there is a
7 question as to what selecting means for example.

8 So let me give you an example. Let's say we say, select all cars that
9 are red that's parked in a particular parking lot. And we define cars to be
10 you know, motor vehicles you know, parked in this particular spot, in this
11 particular parking lot.

12 And if someone gave me a list of the plate numbers of all the cars that
13 are red, would you say that that step is not selecting all of the cars that are
14 red? Do I have to physically drive all the cars that are red to a separate
15 parking lot? I mean, is that -- so doesn't that select have a meaning that's
16 independent of actually, physically corralling all of the things as defined?

17 MR. HOLMAN: Thank you, Judge Chang. Not quite. I would say
18 that the you know, providing the plate numbers of all the cars identifies all
19 of the red cars, but it doesn't necessarily select them. It doesn't selectively
20 separate the red cars, which are the cis-reactive cells with detectable trace,
21 from the other materials in the system, the other cars in the parking lot.

22 And for example, I think it would be helpful if we look at disclosures
23 in the specification on this very topic. If you can turn to Patent Owner's
24 Slide 22 we have a couple of examples where the specification is describing
25 selection. Okay.

1 And you can see here on the left for example, this is from the '848
2 Patent column 19, lines 41 and 48. And the patent describes that the CRCs
3 which display functional interactions must be selected for detection and/or
4 analysis.

5 And when it refers to the filter, or the filtering process the patent says,
6 it's the means employed to selectively separate the desired CRCs.
7 Selectively separate the desired CRCs. Okay.

8 And then on the right there's another example from column 6 from the
9 patent which refers to selection of positive CRCs. And then further down it
10 refers to affinity purification of the library of CRCs.

11 So in each case, the patent is referring to selectively separating the
12 desired cis-reactive cells. And these cis-reactive cells have defined specific
13 criteria. And there's no dispute about what's is required for a cis-reactive
14 cell.

15 And if you look at the plain language of the claims, this is on Patent
16 Owner's Slide 21, this is still consistent with the description that we see in
17 the specification. All right, of course there's Claim 1 on the left there, which
18 recites selecting all cis-reactive cells exhibiting the detectible trace.

19 Dependent Claim 2, which depends on Claim 1, recites again the
20 selecting all cis-reactive cells. And it says, it's accomplished via selective
21 separation or selective detection of the cis-reactive cells.

22 In each case you're either selecting via separating or selecting via
23 detecting the cis-reactive cells away from the other components in the
24 reaction maze. Similarly, dependent Claim 3 depends on Claim 2 and cites
25 that the selective -- excuse me -- selecting all the cis-reactive cells is

1 accomplished by affinity purification. Affinity purification of what? Of the
2 cis-reactive cells exhibiting the detectable trace.

3 Claim 19 similarly recites that the selected detection -- 19 depends
4 from Claim 2 and recites that the selection detection comprises labeling the
5 cis-reactive cells with an affinity reagent. So in each case the plain language
6 of the claims recites just what the express language of Claim 1 states. Is that
7 it's selecting all the cis-reactive cells exhibiting a detectable trace.

8 JUDGE CHANG: So let me, one more question. So you mentioned
9 that there was a distinction between the patent made -- I believe you were
10 quoting the patent between selectively separating and selectively detecting.
11 So doesn't that suggest that you could suggest that you could select the
12 CRCs without physically separating them?

13 MR. HOLMAN: There is a -- the patent does contemplate
14 embodiments of selectively detecting CRCs. But for example, this is in
15 columns 19 to 20 of the patent, there's an example of putting the CRCs onto
16 an array, a microarray. You can hybridize the CRCs onto the array, and then
17 you can label or stain the CRCs that exhibited a detectable trace.

18 But that process is still pulling out or you know, these, the whole, the
19 CRCs away from all of the other materials in the thing. So it's selectively
20 detecting the CRCs by a label or a stain, but it's still a process of selection.
21 You know, isolating or pulling out the CRCs that you want, the ones with
22 the detectable trace, away from the other CRCs or leftover components in
23 the mix.

24 One more point on the plain and ordinary meaning of this selection is
25 found in the original claims in the file history. If you can turn to Patent
26 Owner's Slide 23 please.

1 So here we have two of the original claims that were filed in the
2 application that led to the '848 Patent. On the right you can see original
3 Claim 20 was drawn to a method of detecting functional interactions, much
4 like we see in the granted claims of the '848 Patent.

5 And again, it recites five steps just like '848 Patent's Claim 1. And
6 Step D is the selecting step. It says, selecting all of the cis-reactive cells
7 exhibiting the detectable trace.

8 On the left you can see the original Claim 1 was drawn to a different
9 embodiment. This is embodiment, a method of detecting affinity
10 interactions which are different, it requires a different method from the
11 method of detecting functional interactions.

12 And if you look, you can see that there are different steps. The
13 method of detecting affinity interactions, it has four steps. And it does have
14 a selecting step, but here the selecting step is selecting the plurality of
15 unique associated oligonucleotides. Not selecting CRCs. Right?

16 So the inventors use different language when they intended for the
17 method to select something other than cis-reactive cells. And that same
18 intent is clear from the language of '848 Patent's Claim 1D.

19 Now with that backdrop of selecting all cis-reactive cells, let's take a
20 look at the Kanan reference and what the Petitioner has argued here. If you
21 could turn to Patent Owner's Slide 11 please.

22 All right. So these are snapshots from the Kanan reference. And you
23 know, Counsel for Petitioner put some of their figures up during their
24 presentation. This is Exhibit 1010, Petitioner's lead reference in Grounds 1
25 and 2.

1 And as you can see from Kanan's Figure 1B, which is on the left,
2 Kanan discusses this workflow that you know, comprises putting these
3 complexes together, and then putting them through this selection.

4 And before the selection step, there's a separate disulfide cleavage
5 step followed by an avidin, biotin affinity selection. I'm going to discuss the
6 disulfide cleavage step in detail. But I think it's first, it's important for us to
7 see that this biotin streptavidin selection step, and how Petitioner initially
8 relied on it.

9 If you turn to Patent Owner's Slide 12, this is the extent. This is the
10 extent of Petitioner's argument for mapping Kanan, Kanan's disclosure to the
11 Step D selecting step. This is in the petition, pages 34 to 35.

12 And you can see at the top, the highlighted language there, the
13 Petitioner argues that Kanan discloses after bond formation streptavidin
14 affinity selection for the resulting solution separates biotin related from non-
15 biotin related sequences.

16 Okay. And then below that, under the figure, Petitioner goes on to
17 say, the use of biotin-streptavidin capture would allow selection of only the
18 bond-forming combinations. Which, according to Petitioner, a POSA would
19 have understood as selecting all cis-reactive cells exhibiting the detectable
20 trace.

21 Now Petitioner's problem here is that Kanan's methods require first
22 performing this disulfide cleavage step, and then performing this biotin-
23 avidin selection. And this is what we see on Patent Owner's Slide 17.

24 So the top box on this slide, this is an annotated excerpt of Kanan's
25 Figure 1B. And this is from Dr. Pentelute's declaration. And you can see on

1 the left, is this bond-forming combination before it goes through Kanan's
2 disulfide cleavage and selection process.

3 And the molecules, as you can see there's two -- they have two
4 different oligonucleotides attached. And there's a pink one which is the B
5 strand oligonucleotide, and there's a black one which is the A strand
6 oligonucleotide.

7 And putting this complex through Kanan's workflow, there's going to
8 be a disulfide cleavage which removes the B strand oligonucleotide, that's
9 the pink one, and then there's a selection, the biotin-avidin selection which
10 selects the remaining complex which has the avidin B. And you can see the
11 pink oligonucleotide is missing on the far right there. Okay.

12 Now, if you look at the way the Petitioner has presented it, this is on
13 the bottom, that figure there is, according to Petitioner, that's alleged cis-
14 reactive cell made from a combination of Kanan and Neri. And if you put
15 that same complex through this process, there's going to be a disulfide
16 cleavage, there's going to be a removal of the B strand oligonucleotide, and
17 the resulting complex that gets selected in the avidin-biotin selection process
18 is going to be missing an oligonucleotide strand.

19 And so with the impact of that is that this selection process in Kanan,
20 we can call it a process if you want, that's one of Petitioner's arguments. It's
21 a process. Even if you call it a process, the selection in Kanan doesn't select
22 all the cis-reactive cells having a detectable trace because these molecules
23 that are selected are not cis-reactive cells. They don't meet the defining
24 criteria. Because they're missing an entire nucleic acid moiety, and they're
25 missing half of the associated oligonucleotide.

1 So speaking of selection as a process, let's talk a little bit about
2 Petitioner's arguments in reply. This is on Patent Owner's Slide 19.

3 Now in reply, after Patent Owner pointed out that the you know, the
4 way Petitioner has presented its arguments is that Kanan doesn't teach the
5 selection, the claim selection step. In reply, Petitioner abandons its reliance
6 on Kanan's biotin-streptavidin selection. And now it says, it argues oh,
7 selection is a process.

8 It's a process that begins prior to cleavage of the disulfide bond.
9 That's in Dr. Nelson's reply declaration on the bottom there, Exhibit 1051,
10 paragraph 24.

11 Now if you compare that with Dr. Nelson's original testimony, this is
12 on Patent Owner Slide 20, you can see the juxtaposition of these two
13 arguments from the Petitioner. Dr. Nelson's opening declaration on the left
14 is just like what we saw in the language in the petition.

15 He focuses exclusively on biotin-streptavidin. Says, he's testifying
16 that the use of biotin-streptavidin capture would allow selection of only the
17 CRCs with bond-forming combinations. And then further down he says,
18 therefore in my opinion Kanan discloses selecting all cis-reactive cells
19 exhibiting a detectible trace.

20 Now in reply you can see how he's changed his tune. Now he says, oh
21 Kanan's selection is a process. And now this process begins prior to the
22 cleavage of the disulfide bond. Okay. And this is, I mean this is a new
23 argument. This wasn't in the petition. It wasn't in Dr. Nelson's opening
24 declaration. And it's not merely a responsive argument expanding, or
25 clarifying a previous position.

1 Petitioner is running on a different disclosure in Kanan now.
2 Something that occurs before the disulfide cleavage. Some point in time
3 before the disulfide cleavage is allegedly teaching claim element 1D.

4 JUDGE CHANG: So let me back up a little bit. On Slide 20, the
5 quote you were just talking about. Does the biotin-avidin capture, that
6 occurs before the disulfide cleavage. Am I correct?

7 MR. HOLMAN: No, Your Honor. In following Kanan's workflow
8 the disulfide cleavage happens first, and then there's the biotin-streptavidin
9 capture.

10 JUDGE CHANG: Okay.

11 MR. HOLMAN: And that's the crux of Petitioner's problem here. Is
12 that following Kanan's workflow, as Petitioner has explicitly said a person of
13 skill in the art would do, they're going to -- they're going to perform the
14 disulfide cleavage step first, which chops off the B strand oligonucleotide,
15 and then they're going to do this biotin-streptavidin selection.

16 And so the thing that they're selecting, the complex that they're
17 selecting is not a cis-reactive cell.

18 JUDGE CHANG: Okay. I understand your argument.

19 MR. HOLMAN: All right. So in support of Petitioner's newfound
20 view of selection, they point to several different disclosures in the Patent to
21 argue that well, the Patent contemplates various ways of selection.

22 We have this on Patent Owner's Slide 24 please. Now Petitioner, and
23 you can see this is from the reply page 2. Petitioner argues that, well the
24 specification describes various ways of selection such as selective
25 amplification with PCR, or oligonucleotide tag array paired with labeled
26 affinity reagents.

1 And therefore, you know, construing this claim term, or this phrase,
2 claim element as you know, plain and ordinary meaning to select all cis-
3 reactive cells exhibiting a detectable trace would somehow improperly
4 exclude these embodiments.

5 But if you look at the actual disclosures that Petitioner relies on, they
6 don't support Petitioner's argument. So the first example we have on this
7 slide is from column -- the Petition relies on disclosures in column 19 of the
8 '848 Patent, lines 7 through 9.

9 And you can see in the text excerpt on the bottom here, this disclosure
10 comes from the '848 Patent's discussion of selection methods related to
11 affinity interactions. Right?

12 This is a different embodiment of the '848 Patent. It's not even
13 claimed -- it's not even in the claimed method. And as we saw from the
14 original claims, selection meant -- the selection process for detecting affinity
15 interactions doesn't even involve CRCs. Okay.

16 The next section Petition relies on is from column 20. This is on Slide
17 25 please.

18 Now here Petitioner relies on disclosure related to a microarray
19 embodiment. And this is column -- in the '848 Patent it's in column 20, lines
20 31 to 39. And we have this text here in the bottom. You can see the
21 language in the specification.

22 And so here, the '848 Patent says that the CRCs can be hybridized to a
23 DNA oligonucleotide tag array. That's all it says. It says that the CRCs can
24 be hybridized to an array. And then further down the patent refers to the
25 array with the CRCs that can be stained or labeled with an affinity reagent.

1 So all it's saying here is that you can add the CRCs to an array.
2 Hybridize the CRCs to an array. All right. Nothing more.

3 Petitioner's expert, Dr. Nelson speculates in his reply declaration, this
4 is Exhibit 1051, paragraph 21. Dr. Nelson speculates well, this disclosure
5 must mean that the CRCs are broken apart, or that they're de-hybridized or
6 denatured to add them, hybridize them to the array.

7 But the patent doesn't say that. It doesn't say anything about that.
8 And in fact, Dr. Nelson admits in that same paragraph, 21, Exhibit 1051, that
9 if the NAMs, the nucleic acids moieties of the CRCs are single stranded, the
10 reaction mixture is added to the microarray.

11 And that's simply, that's consistent with the disclosure in the patent
12 here. That you can add the CRCs to the microarray.

13 Finally, Petitioner also relies on disclosures from column 30 in the
14 '848 Patent. If you could turn to Slide 26 we have an example of this
15 disclosure.

16 Now the disclosures in column 30 come from the '848 Patent's
17 example 5. And if you read through example 5 you'll see that that
18 experiment, or that method that's described there is not the claimed method.
19 It's not an embodiment of the claimed method.

20 In example 5, the interaction that's being detected is called a thiol
21 dimerization. And if you read through example 5 you'll see that it describes
22 first inducing this interaction, inducing this thiol dimerization.

23 Then there's an association of the nucleic acid moieties, and then -- by
24 ligation. And then there's a detection step. So there's an interaction, then an
25 association, and then a detection.

1 And if you look at the claim method, that's not what's recited. In the
2 claim method it's an associated first, in forming the CRCs. Then there's an
3 interaction. And then there's the selection of the CRCs, and then there's a
4 detection.

5 I'll further note with example 5, it doesn't refer to or describe selecting
6 CRCs at all. It doesn't even use the term CRCs in example 5.

7 So contrary to Petitioner's argument, construing the claims by the
8 plain and ordinary meaning to require selecting all cis-reactive cells
9 exhibiting a detectable trace does not improperly exclude embodiments of
10 the invention.

11 All right. If you could turn to Slide 31. Final note on this is that you
12 know, even if you want to consider Petitioner's you know, shifting
13 arguments in the reply, they still haven't shown that this method teaches or
14 suggests the elements of Claim 1D.

15 According to the Petitioner, this is from this -- the figure is from Dr.
16 Nelson's reply declaration in paragraph 30. And Dr. Nelson says that this is
17 a depiction of how the bond forming combination in Kanan and Neri would
18 look after polymerization and the selection process.

19 So they've done the polymerization, they've done a selection, but they
20 haven't done the detection yet. And he says it will be visualized as follows.
21 And he shows this image here. And you can see here, this image is not a cis-
22 reactive cell. Right?

23 It's missing an entire nucleic acid moiety. And it's missing -- and so it
24 doesn't comprise two interactors. It can't. And it's missing half of the
25 associated oligonucleotide. There's only one purple region there, when the
26 original cis-reactive cell which had -- allegedly had an associated

1 oligonucleotide. That was formed from the two purple regions that were
2 hybridized with each other.

3 So even if you consider Petitioner's arguments on the merits, they still
4 haven't shown that this art teaches the selecting step 1D.

5 I'd like to address step 1E now. And in particular, the polymerization
6 issue. Judge Chang had some questions on that earlier. If you could turn to
7 Slide 33 please.

8 So as Patent Owner's argued in our Patent Owner's response and
9 reiterated in our sur reply, Petitioner's arguments fail to show that Kanan and
10 Neri teach or suggest Step E for at least two reasons.

11 The first is really straight forward. Because Step E requires the
12 completion of performing Step D. Right? Step E says, subjecting the
13 associated oligonucleotides from the cis-reactive cells that were selected in
14 Step D. Okay. And if the you know, the art doesn't teach or suggest Step D,
15 it likewise doesn't teach or suggest performing Step E.

16 The second issue with -- the Petitioner has here, is that as presented in
17 the petition, there's no explanation of how this polymerization step would
18 have been implemented in the proposed combination.

19 And as I mentioned, Judge Chang, you had some discussions with
20 Counsel for Petitioner on this, on the polymerization issue. And I believe
21 you asked if you know polymerization was discussed anywhere in Claim 1
22 other than the motivation to combine, the reasonable expectation of success
23 discussion.

24 And we heard from Counsel for Petitioner, he pointed to the
25 disclosures in the Petition about reasonable expectation of success, and
26 motivation to combine. But there was no real -- there was no discussion of

1 when is this really happening, aside from the discussion in Claim 17's
2 association via polymerization. Right?

3 So when we pointed this out in our Patent Owner's response, that's
4 when Petitioner was on its heels, backtracking saying, oh well we discussed
5 polymerization. It happens at the time of association because that's from
6 Claim 17.

7 So they're you know, they're relying on this dependent claim
8 discussion, pushing that up to address Claim 1. But I want to --

9 JUDGE CHANG: So, Counsel, let me -- so let me ask a question
10 because I think Petitioner -- and so, my question is also, well, Claim 17
11 depends from Claim 1, so all of the discussion of Claim 17 sort of applies to
12 that more specific embodiment of Claim 1. So, for instance, are you
13 suggesting that we can find Claim 17 invalid or unpatentable, but then find
14 Claim 1 patentable because there was not a specific use of the word
15 polymerization in that claim discussion?

16 MR. HOLMAN: Well, so, we -- Patent Owner agrees that Claim 17,
17 of course, depends from Claim 1, and recites that --

18 JUDGE CHANG: I think your microphone might be off. I can't hear
19 it very well. Can someone check?

20 MR. HOLMAN: Oh. I think I may have accidentally pushed a
21 button. Sorry. Can you hear me now?

22 JUDGE CHANG: Yes.

23 MR. HOLMAN: So, I was just saying, Patent Owner agrees that
24 Claim 17 depends from Claim 1, and Claim 17 recites that the association is
25 via polymerization. But Patent Owner's, our point here is that even if you --
26 even if the Board wants to credit Petitioner's discussion of Claim 17 and

1 push that back up to Claim 1, it's still insufficient. They still don't explain
2 how this works. They still don't explain how this fits together. And
3 according to Federal Circuit law, such as *Personal Web v. Apple*, Petitioner
4 must explain how the combination of references is supposed to work. All
5 right.

6 And so, I think one of the slides I'd like to show you that can really
7 show that, you know, show our point here is on Patent Owner's Slide 34.
8 Petitioner pulled this slide up earlier in their presentation. And one of the
9 things Counsel for Petitioner noted is that this starts at Step C. And that
10 might be correct, but that's the figure that Petition presents, page 33.

11 But Your Honor, Step C, is already -- the CRCs have already been
12 formed. This is after the CRC has been formed. That happens in Step B. In
13 Step C, the CRCs are subjected to the reaction conditions. And according to
14 Petitioner, polymerization was already supposed to have happened at the
15 time of forming the CRCs, at the time of association. And so, that was our
16 point. We pointed this out.

17 We're walk through the Petition's workflow of when they're -- how
18 they put these molecules together. Then they, you know, submit their -- or
19 subject them to functional interactions. That's over on the right, Petition,
20 page 33. And then they have this bond-forming pair, Petition at page 34.
21 These are Petitioner's figures here. And there is no evidence that there is a
22 polymerization, right? That extra identification sequence element is not
23 present. And then you put that through the selecting step on the left and step
24 -- Petition at page 34, and on down to the analysis step.

25 And so, that was our point in the Patent Owner's Response is that,
26 okay, they say a POSA would be motivated to do polymerization in the

1 motivation to combine discussion, but where is that happening? I mean, you
2 know, when is it happening? How is it happening? Okay?

3 And if you want to credit the discussion of Claim 17, as the -- to say
4 that the Petitioner gets credit for arguing that it happens at the time of
5 association, even that, Your Honors, is inconsistent. For example,
6 Dr. Nelson -- and this is on Patent Owner's Slide 45 -- Dr. Nelson, on one
7 hand, says that -- this is on the left from his reply declaration, and he says,
8 oh, association via polymerization would occur at the time of association.
9 And that's paragraph 9. But then, elsewhere in his declaration, he refers to
10 polymerization happening after formation of the CRC, so after association.

11 So, our point here is really that the Petitioner is -- they're inconsistent.
12 Their arguments are all over the place. They're changing. They're pivoting,
13 and it's this moving target approach that is foreclosed by the law, by statute,
14 and by legal precedent. Now, the result of this is -- there's two problems
15 here.

16 So, first of all, let's look at Patent Owner's Slide 36, please. As
17 presented in the petition, you know, if you walk through the workflow of the
18 petition, where we show that it doesn't look like a polymerization is even
19 happening, this would be the result, right? And we explained this in our
20 Patent Owner's Response that the B strand oligonucleotides can be cleaved
21 off. That's on the -- it's on the top there. And the thing that gets -- the
22 molecule that gets selected -- or the structure that gets selected is missing,
23 not only missing an entire nucleic acid moiety, but it's missing one of the
24 identification sequence elements. And so, because of that, without this
25 polymerization, there's not going to be the ability to detect the two
26 identification sequence elements, which is required as part of Step E.

1 Now, of course, the Petition says, oh, no, no, there should be
2 polymerization there. But that, Your Honors, that argument also fails to
3 meet Petitioner's burden. So, first, let's go to Patent Owner's Slide 40,
4 please. All right.

5 Now, as presented in the petition, this is the figure on the left, and
6 according to Petitioner, this is a cis-reactive cell that's been, you know, it's
7 been created, and it's been subjected to conditions where there's a functional
8 interaction, so the A6 and the B9 molecule have formed this bond. And
9 then, according to Petitioner, there's a polymerization step somewhere that
10 would copy over the other -- the B strand identification sequence element.

11 But as Dr. Pentelute explains, as presented in the petition, this
12 structure is not even conducive to doing a polymerization step because it
13 doesn't have the two other nucleotides to the left of the purple region are not
14 hybridized together, or at least that's how they originally depicted it; they're
15 not hybridized together. And so, instead of forming this nice, you know,
16 clean structure on the left, it's actually going to splay out in this Y-shaped
17 structure, which Dr. Pentelute explains is incapable of a polymerase
18 extension reaction.

19 Now, Petitioner says, actually, that figure is not correct; the figure on
20 the left is not correct. If you look at Patent Owner's Slide 41, we have the
21 evidence of this changing tune here. So, Dr. Nelson, the original figure, you
22 can see on the left, and we circled this region, which indicates these two
23 strands are not hybridized together, because one of the strands has vertical
24 lines coming from it, and the other strand does not. And we asked
25 Dr. Nelson about this depiction at his deposition, and he said, yeah, when

1 there is only vertical lines on one strand and not on the other, that indicates
2 that it's not hybridized together.

3 Now, only in, you know, on redirect, presumably after meeting with
4 Counsel, Dr. Nelson changes his tune, and now he says, oh, actually, that
5 should be hybridized together, that region; I should've drawn that as
6 hybridized after all. And so, and of course, in the reply, Petitioner's reply,
7 and Dr. Nelson's reply declaration, they now present it as hybridized
8 together.

9 Well, we asked Dr. Nelson about this newfound hybridization region
10 during recross, and Dr. Nelson testified that this what we call a universal
11 hybridization region, meaning any B strand oligonucleotide can hybridize to
12 any A strand oligonucleotide at this region, okay? And what the problem is
13 for Petitioner has here is that this creates significant issues with cross-
14 hybridization. This is depicted on Patent Owner's Slide 43.

15 So, now, because the Petitioner has modified to have these two
16 regions that are universally complementary, and you can see that on the left.
17 These are depicted as the Hyb, the purple regions, Hyb1A and 1B, that's the
18 alleged self-assembly region. So any strand A can hybridize with any strand
19 B at the purple region. And now we have an additional region, Hyb,
20 Dr. Pentelute labeled as Hyb2A and Hyb2B on the left. And again, any
21 strand A can hybridize to any strand B at the Hyb2 region as well. And the
22 result of this is a mishmash of, you know, spaghetti strands all cross-
23 hybridized with each other. You're going to get interactors hybridizing with
24 other interactors.

25 And when you perform this polymerization step, again, where, you
26 know, if you want to give Petitioner credit for discussing polymerization, the

1 result is false positives and false negatives. And this is shown on Patent
2 Owner's Slide 44.

3 On the top left, this is where the polymerization would happen, right?
4 It's going to copy this pink B strand, or pink code B, onto the A strand,
5 when, in fact, the interacting molecules in this figure were green B and
6 orange A. And so, the result is, you know, the feedback, or readout, shows
7 that the pink B interacted with orange A, but that's not -- that's not correct,
8 so that's false positive. And in fact, the orange A interacted with green B,
9 but you missed that detection because of all this cross-hybridization
10 problems, so it's a false negative.

11 And as we explained, and Dr. Pentelute explained, a person of skill in
12 the art would have seen this and realized that this is not a -- it's not an
13 effective design. It's not going to work. It's not going to be a useful assay.
14 It's going to provide completely unreliable results. And so, for that reason,
15 they wouldn't have been motivated to make this proposed combination in the
16 first place, nor would they have had a reasonable expectation of success.

17 I'd like to briefly address Claim 16. This is for Ground 2, with the
18 combination of Kanan, Neri, and Famulok. So, if you could, turn to Patent
19 Owner's Slide 51, please.

20 Now, Claim 16 recites that association is via ligation. And according
21 to Petitioner, the POSA is going to modify the Neri embodiment depicted in
22 Neri's Figure 7, here, and that's on the bottom right. But as we explained in
23 our Patent Owner's Response, and again in our Sur-reply, this embodiment
24 in Neri, it's already associated, right? These, you know, alleged interactors,
25 they're already associated by hybridization. You can see that by the
26 horizontal lines between these two oligonucleotide strands.

1 But according to Petitioner, you're going to form this structure, and
2 then you're going to ligate A, maybe, the ends of A of B together using the
3 splint oligonucleotide from the Famulok reference. So, but as we explained,
4 this structure is already hybridized, so it doesn't teach or suggest association
5 via ligation. If anything, it says association by hybridization.

6 Now, in response, the Petitioner argues that, well, the patent, '848
7 Patent, contemplates doing some hybridization before you do this ligation.
8 And Petitioner relies on the '848 Patent's Figure 5. If you could turn to our
9 Slide 52, we have this figure here.

10 Now, Petitioner argues that Figure 5 depicts these embodiments where
11 there's going to be some hybridization between the interactors, before the
12 ligation. In fact, Dr. Nelson goes so far as to testify that Figures 5 -- Figure
13 5(a), (b), (d), (e), there's some prior association, i.e., hybridization, between
14 the interactors before the ligation. That's Exhibit 1051, paragraph 72.

15 Now, we've annotated this figure in our Sur-reply to show the nucleic
16 acid moieties are in purple -- or excuse me -- in blue and red. And you can
17 see from, in Figures (a), (b), (c), (d), here, that the blue and the red nucleic
18 acid moieties are not hybridized with each other. There's no hybridization
19 between the interactors here.

20 But in contrast, Figure 5(e), while there is some hybridization between
21 the interactors, that's taking place at the site, at the location of the ligation.
22 That is, the ligation takes place at the site of association or hybridization.
23 And that's consistent, actually, through all five of these embodiments. Let
24 me show this on Slide 53, where we've highlighted this on the left. Again,
25 this is Figure 5 from the '848 Patent, and in each case, you can see that the
26 ligation takes place at the site of association between the NAMs. Whether

1 they're hybridized with each other or not, ligation is taking place at the site
2 of association.

3 Now, if you look at Petitioner's proposed embodiment -- this is the
4 Famulok ligation embodiment -- the ligation takes place with the splint
5 oligonucleotide on the left of the structure, which is unrelated to the
6 association. All right. The association is highlighted there, where the
7 Hyb1A and Hyb1B hybridize together. So this combination, even if you
8 give Petitioner credit for putting it together, it doesn't teach association via
9 ligation.

10 Moreover, as Dr. Pentelute explains, this proposal also is fraught with
11 its own technical roadblocks that a POSA would have expected and would
12 have deterred their approach from the get-go.

13 JUDGE CHANG: Sorry, Counsel. Before you go there, let me ask.
14 So the claim says it's a method of detecting functional interaction
15 comprising. So, is there any problem with having multiple methods of
16 association, or is Patent Owner's argument that the ligation is not, in fact, an
17 association in the proposed Petitioner's proposal?

18 MR. HOLMAN: Yes, Your Honor. So, if you -- if we could, go back
19 to Slide 51, just so we can have the claim language there.

20 So, what's important here is that the Claim 16 says, wherein,
21 association is via ligation. All right? It doesn't say, wherein, the association
22 comprises ligation. The association -- for this dependent claim, association
23 is via ligation. And there's only one association. That's when these -- the
24 nucleic acid moieties become associated with each other for forming the cis-
25 reactive cells.

1 If you could, go back to Slide 55, please. The final point on Ground 2
2 is -- and Dr. Pentelute explains this -- is that there is some severe technical
3 flaws with this proposed combination, this ligation embodiment. Again, if
4 you look on the left, that's Neri's Figure 7, and Petitioner argues that a
5 person of skill in the art is allegedly going to ligate the ends A and B
6 together with the splint oligonucleotide.

7 And so, there's two paths here, two possibilities. One is that the ends
8 of A and B are unique. And so, in that case, you'd have to have a unique
9 splint oligonucleotide made for every pair of A and B. Okay. And that
10 defeats the entire purpose, according to Petitioner, of making this
11 combination in the first place, to create this combinatorial, you know,
12 efficient way of detecting these interactions. You're going to have to make
13 it, and it's going to be really tedious, time-consuming, and it defeats
14 Petitioner's stated purpose.

15 Option two is making the ends universal, so such that any A and B
16 can hybridize with a splint -- with a common splint oligonucleotide. And as
17 Dr. Pentelute explains and depicts in his figure here, you can see -- this is in
18 Exhibit 2008, paragraphs 166 and 167 -- with a common splint
19 oligonucleotide in common A and B hybridization sequences, you're going
20 to get cross-hybridization. You're going to have interactors hybridizing with
21 each other. This is a simplified version of just two alleged CRCs connecting
22 to each other. It could be a third, fourth. It could create an entire, again,
23 spaghetti junction of cis-reactive cells, and the result is useless data,
24 unreliable data filled with false positives and false negatives.

25 The Petition doesn't address any of these problems in the petition.
26 And even in reply, Petitioner's argument amounts to, oh, a POSA could

1 figure it out. That's essentially what they said: A POSA would have been
2 able to figure out conditions to prevent unintended hybridization.

3 But as I mentioned earlier, for example, you can look in *Personal Web*
4 *v. Apple*, the 994. The Petitioner must explain how the combination of
5 references is supposed to work, and in complex technologies like this, more
6 explanation is necessary. *Personal Web* says it. They say if the technology
7 is simple, maybe a brief explanation is all that's needed. If the technology is
8 complex, more explanation is needed. And that explanation is lacking in the
9 Petition and is lacking in the reply.

10 Now, with the remaining few minutes, I'd like to address Petitioner's
11 Grounds 3 and 4, please. If you could, turn to Slide 58.

12 JUDGE CHANG: I think you might have turned off your mic again.

13 MR. HOLMAN: Oh, gosh. Apologies.

14 JUDGE CHANG: And before we move on from Ground 1 and 2, I do
15 have one question, and I know you reserved some time, so you can also
16 answer it then.

17 But going back to the definition of cis-reactive cell, the claim
18 construction issue we started with, I was just looking at the patent again.
19 And on column 9 -- this would be Exhibit 1001, column 9, line 35 -- it says
20 the cis-reactive cell prefers an association of at least two interactive moieties
21 joined by an associated oligonucleotide. In the specific embodiment, a CRC
22 comprises two interactors.

23 So, it sounds like, seems to me, that that suggests that the two
24 interactors is not required, that you could have something called two
25 interacting moieties. Do you have -- does Patent Owner has a position of
26 what two interacting moieties refers to?

1 MR. HOLMAN: I see that, Your Honor. So, I think the, you know,
2 this disclosure, and we may want to address some of this in our rebuttal
3 time, but the disclosure refers; it says that a cis-reactive cell refers to an
4 association of at least two interacting moieties. All right. So that's -- and if
5 you look at the definitions of interactors, that is found in the specification.

6 JUDGE CHANG: It's right above it. It's right --

7 MR. HOLMAN: Right above it, yeah. Column 9, lines 33 to 34, says
8 an interactor refers to at least one MOI coupled with least one NAM, right?
9 So, I think, in that second sentence there, lines 37 and 38 of column 9, where
10 it says the specific embodiment, CRC comprises two interactors, I think it's
11 saying the specific embodiment is that that CRC has two interactors, as
12 opposed to more than two, because, you know, the CRC refers to an
13 association of at least two.

14 So you can have more than one -- or more than two interactors, but
15 the problem with Petitioner's embodiment here, with this ligation
16 embodiment, is that these CRCs, if you run the polymerization and the
17 analysis Step E, you're still, you're going to get these false positive and false
18 negative results because of the cross-hybridization between these interactors
19 the way the Petitioner has designed it. This is different from the way that
20 the '848 contemplates making these CRCs.

21 JUDGE CHANG: Okay. So the Patent Owner's position currently is
22 the interacting moieties is the same as interactors; is that correct?

23 MR. HOLMAN: Yes, yes, Your Honor, and that is how Patent Owner
24 reads it. The interactor, when it's referring to interacting moieties, it's
25 referring to interactors.

26 JUDGE CHANG: Okay. Thank you.

1 MR. HOLMAN: In the last few minutes, I'd like to address claim --
2 Grounds 3 and 4, please. And this is, as we said, we're on Slide 58.

3 So, Grounds 3 and 4, of course, Petitioner relies on the combination of
4 Baez and Landegren for Ground 3, and then they bring in a third reference,
5 called Freskgard, for Ground 4. And of course, the Petitioner purports to
6 provide a different meaning of the claim terms in this argument, based on --
7 according to Petitioner, it's based on Patent Owner's application of the
8 claims and related litigation with Petitioner.

9 And I believe, Judge Chang, you asked, you know, is this is not plain
10 and ordinary meaning, so if the Board applies it or doesn't apply plain and
11 ordinary meaning, what happens to Grounds 3 and 4? Frankly, Your
12 Honors, it doesn't matter what meaning you apply to the claim terms for
13 Grounds 3 and 4. Under any construction, whether it's plain and ordinary
14 meaning or something else the Petitioner argues, the Petition has failed to
15 show that this -- that their art combination teaches or suggests Claim
16 Elements 1(a), 1(c), and 1(d).

17 With the remaining time, I'd like to focus on -- excuse me. Not 1(c).
18 1(d) and 1(e). I apologize. I'd like to focus on 1(d), the selection step in
19 Grounds 3 and 4. If you could, turn to Slide 64, please.

20 Now, Petitioner's problem here, with showing that Baez teaches the
21 selection step, is based on a fundamental mischaracterization of Baez's
22 disclosures of what an analyte-specific amplicon is. Right, and Baez defines
23 it explicitly. This is on the left, Exhibit 1003, column 9, lines 27 to 31.
24 Baez states that an analyte-specific amplicon, or an ASA, refers to the
25 nucleic acid product formed by joining the two assay nucleic acid labels,
26 right?

1 So, an ASA is a nucleic acid product. Compare that with a cis-
2 reactive cell of the '848 Patent. That's on the right there. You can see a cis-
3 reactive cell refers to an association of at least two interactor moieties,
4 joined by an associated oligonucleotide. And then an interactor, of course, is
5 at least one MOI coupled to one NAM. So an ASA is a nucleic acid
6 product, and of course, a cis-reactive cell comprises two interactors.

7 Now, if you turn to Patent Owner's Slide 65, this is where Petitioner
8 runs into problems. They repeatedly and consistently conflate these two
9 terms, equating cis-reactive cells in the patent with ASAs in Baez. Again
10 and again, this is in the petition. It's in Dr. Nelson's reply declaration, and
11 it's in the reply brief.

12 And on the next slide, Slide 66, Petitioner doubles down and actually
13 goes so far as to say that an ASA (circled) -- which is in the box here -- is
14 the complex with the two antibodies connected via ligation of their nucleic
15 acid labels. But if you compare that with the definition of Baez again, at the
16 bottom here, ASA is not a -- it's a nucleic acid product. It's not the complex.

17 And the last point, I realize I'm a few seconds over, but the last point,
18 I just want to explain why this matters. This is on Slide 63, the Patent
19 Owner's Slide 63. It matters because Baez only teaches detection of ASAs,
20 not selection of cis-reactive cells. And you can see this. This is in Baez,
21 column 17, where he refers to detection, detection of the nucleic acid
22 products, refers to detection strategies, refers to facilitating detection. Again
23 and again and again, it's detecting the ASAs. And even if the Board were to
24 interpret this as some form of selection, it's still, even then, only selecting
25 ASAs. It's not selecting cis-reactive cells, which is required by Claim 1(d).

1 I'm about a minute over time, so unless Your Honors have any
2 specific questions, I'll save my remaining time for rebuttal. Thank you.

3 JUDGE MITCHELL: Thank you.

4 Whenever you're ready.

5 MR. PLATT: Okay. All right. So, first off, I just want to address
6 one thing. This has not been a moving target, as Patent Owner alleges. The
7 arguments that were made in reply are fully proper under the rules, and that's
8 because a Petitioner's reply may respond to arguments raised in the patent
9 owner's response. And that is exactly what we've done here.

10 We've provided responsive arguments to further explain how the
11 references teach the limitations based on Patent Owner's arguments and
12 merely expanded on the petition's existing theories. Indeed, most of the
13 issues that were raised on -- in Patent Owner's Response were raised after
14 trial was instituted in this case.

15 So, if we could go to Slide 26, so I want to start by talking a little bit
16 about the selecting step that the Patent Owner was discussing.

17 And if we actually go back to Slide 25, Jessie, and we can start there.

18 And looking at Kanan Figure 1(b), here on the right, and look at
19 what's happening here. As you can see, it starts out with non-bond-forming
20 combinations and bond-forming combinations. And in the first part of the
21 argument, we talked about how important it is to note that they're called
22 combinations, right? And the process in Kanan is one that is -- does this,
23 you know? We talked about being clever, right? It has this biotin attached
24 to it to allow for you to be able to select out the bond-forming combinations.

25 And so, that's why, when you look at the -- you look at the top; you
26 have non-bond-forming combinations and bond-forming combinations. You

1 then have -- and this is what's called -- it calls it a one-pot selection and
2 detection process, and that's because it's all done in the same solution. What
3 happens is you have this disulfide bond cleavage that then cleaves that
4 disulfide bond and then allows for you to get -- be left with just those bond-
5 forming combinations, right, that have that specific nucleic acid on it with
6 the two identification sequence elements.

7 Now, and it's important to note that when you look at Kanan, what is
8 it doing? It is selecting for bond-forming combinations. If it was not
9 selecting for bond-forming combinations, why does it call it bond-forming
10 combinations, right? It would no longer be a combination, right? That's
11 what's shown is after that reaction takes place.

12 Now, on the left-hand side is what the CRC would look like as
13 reflected in Dependent Claim 17, right, where there has been
14 polymerization, and the A strand includes both identification sequence
15 elements.

16 Now, if we go to Slide 26, okay, you'll see that then through that
17 process, the Kanan and Neri combination, it preserves the associated
18 oligonucleotide nucleotide that has both sequences on it. And that's what
19 goes on to Step E.

20 Now, Patent Owner calls this destroying the CRCs with a functional
21 interaction, but that's not consistent with Kanan's process, which it
22 ultimately results in these combinations that are selected.

23 And the real problem is that if you did not -- if you did not do the
24 disulfide cleavage as part of this, you would never be able to separate out --
25 you would never be able to select for the bond-forming combinations
26 because you would never have that disulfide bond cleavage. So you'd have

1 the non-bond-forming ones that are floating around. You'd have the bond-
2 forming ones that were floating around. And all of those would bind to
3 avidin, and ultimately, you wouldn't get any helpful information in Step E.
4 But what the Kanan workflow does is it allows for selection of the CRCs
5 that have that detectable trace.

6 And if we go to Slide 27 and talk about what the plain and ordinary
7 meaning of selecting is, what I think I heard Patent Owner argue is that
8 selecting means selectively separate, right? But that's not what the claim
9 language says. The claim language says selecting all the CRCs.

10 And in fact, the Patent Owner did go through some of those, but it's
11 important to recognize that selecting is very broad in terms of what it
12 includes. It's not limited as Patent Owner seems to suggest, or actually
13 explicitly argues, that it requires this single affinity capture event. That's not
14 the plain and ordinary meaning of selecting.

15 And while Patent Owner points to other portions of the specification
16 that talk about whether it's affinity interactions or other types of interactions
17 that take place that are ultimately selected, the word selecting is not -- the
18 plain and ordinary meaning of selecting does not change depending on sort
19 of what you are selecting for. And when we look at the claim, what it's
20 ultimately selecting for is all CRCs so that it can go on to Step E, where that
21 associated oligonucleotide is analyzed.

22 Now, when we look at the spec, it has all these different examples of
23 selecting, and if we turn to Slide 28, these were the dependent claims. And
24 it's important to recognize that -- and I think, let me just pause for a second
25 on Dependent Claim 2, because that's important. And Dependent Claim 2

1 was actually amended during prosecution, and that language was added
2 during prosecution.

3 And let me -- now, what is important there is during prosecution,
4 when they added that language, they added selective separation and selective
5 detection. And what they said -- and this is important -- the techniques were
6 well known in the art. And that's what we have shown here on Slide 48.
7 And that is true. Selecting is well-known in the art. And in fact, that's one
8 of the ways that Neri -- I'm sorry -- Kanan actually includes a method of
9 selecting for cis-reactive cells that have that detectable trace.

10 Now, if we could go back to the dependent claims, and what we see
11 there is, there are a wide variety of different types of selecting that takes
12 place, selective separation. So we know that when Patent Owner argued
13 selecting means selective separation, well, it could also mean selective
14 detection. It could also mean affinity purification. It could also include
15 labeling. It can also include modification that allows for selective detection.

16 And in fact, when we asked Patent Owner's expert about this -- this is
17 Slide 29 -- he agreed that there is all these different ways in which selection
18 can occur, and that selection can be a procedure. In fact, what Patent
19 Owner's expert said is the specification provides many, many possibilities
20 for selection, and the list goes on. So this idea that selecting is limited to
21 only selective separation is just incorrect.

22 JUDGE CHANG: So, Counsel, would you -- I don't think Petitioner
23 has proposed an explicit definition. I know you rely on the ordinary, plain
24 and ordinary meaning. Would you say Petitioner's construction might be
25 something like -- is there a construction that you would propose for
26 selection? What is that? What does that mean to Petitioner?

1 MR. PLATT: Well, I think, within -- so the plain and ordinary
2 meaning is what's been provided. And in terms of the question, I think, that
3 was raised in Patent Owner's reply, is whether selecting should be limited to
4 just this affinity capture event. If there's -- when we're looking at what the
5 plain and ordinary meaning of selection is, it's similar to Your Honors
6 example relating to, you know, selecting red cars, right? There can be a
7 process that's involved in it. There can be a step of identifying it. It's not
8 limited in the way that Patent Owner suggests.

9 The ultimate goal -- and this is what's important -- is, in the context of
10 Claim 1, overall, right, the claim's stated purpose, the method of Claim 1,
11 right, is a method of detecting functional interactions between at least two
12 molecules of interest. And so, in Step D, you have to select all cis-reactive
13 cells exhibiting the detectable trace, and then Step E is subjecting the
14 associated oligonucleotides from the cis-reactive cells selected in Step D to
15 an analysis that permits detection of the at least two identification sequence
16 elements.

17 So, when we're looking at selecting, the goal is to be able to, like in
18 the Kanan workflow, to be able to see those two identification sequences so
19 that you can identify it.

20 And if we could, go back to the Kanan workflow diagram, Jessie. I
21 believe that's Slide 26.

22 And when we look at it, the -- one of the things to keep in mind with
23 respect to the Kanan workflow, and this is -- this was one of the reasons why
24 you put the self-assembly sequences in. As you may recall, it's, you know,
25 we're looking at -- if we've got 100 substrates of A and 100 substrates of B,
26 we've got, you know, I think it's 10,100 different sequences in there, right,

1 that are all mixing together. And you have to have both the A and the B
2 come together, right?

3 But because of the workflow in Kanan, right, it has its A strand, which
4 is ultimately what gets selected in these bond-forming combinations after the
5 disulfide cleavage. Keep in mind that in Kanan, it has both those. The A
6 strands have both the B9 sequence identification element on it and the A6
7 identification sequence element on it, okay? So, when it goes through, that's
8 what's allowing it then to detect that A6 and B9 have gone through this
9 bond-forming reaction.

10 But when you use the self-assembly sequences that takes place when
11 you incorporate Neri into Kanan, right, and after polymerization, now you
12 have this double-coded code on both strands of the nucleic acid, which then,
13 just like in Kanan, you, now, what comes out as part of those bond-forming
14 combinations includes what's shown on the right, identification sequence
15 element A. Here, it would be A6, for example, and identification sequence
16 B, B9 in this example. Now, if --

17 JUDGE CHANG: Sorry. I think you might have answered one of my
18 questions from earlier. So, going back to the discussion we were having
19 about how can you be sure that the A6 -- let's say the A12 strand does not
20 have the -- an A pool nucleotide does not have both A12 and B3 on it; it's
21 not detected. You're saying it's because when you cleave the disulfide bond,
22 essentially, the A12 would also fall away, so there will only be the A -- so
23 the A6 nucleotide with the A6 and B9 sequence elements are the only ones
24 that would remain, be selected.

25 But, so let me ask another question. So, in that case, you are doing
26 polymerization for a lot of combinations that doesn't have a bond-forming

1 reaction. Is that correct? And if that's so, how does that, you know -- how
2 does that interact with your efficiency argument for the motivation to
3 combine?

4 MR. PLATT: I think, when you look at Kanan and the fact that it's a
5 one -- it's a one-pot selection method, it actually is consistent with that
6 efficiency, and that you're just doing the polymerase reaction that one time.
7 And it is what actually allows for you then to be able, again, after the
8 disulfide cleavage, to be able to select for those bond-forming combinations
9 or CRCs that have that functional interaction.

10 JUDGE CHANG: Okay. Thank you.

11 MR. PLATT: And we've talked a bit about polymerization and
12 Dependent Claim 17. So, one of the things that we raised, and we've talked
13 about whether Dependent Claim 7 -- 17 is obvious. And as we discussed
14 earlier, there's the little -- there's Federal Circuit authority, right, that says by
15 definition, an independent claim is broader than a claim that depends from it.
16 So, if a dependent claim reads on an embodiment of the claimed invention,
17 the corresponding independent claim must cover that as well. And that was
18 the *Littelfuse v. Mersen* case.

19 That concept also applies in the PTAB, and this is in *Vizio v. Polaris*,
20 and this was IPR2024-0073, and it's Paper 32. And I'm happy to provide a
21 copy to Judge Mitchell if that would be helpful.

22 JUDGE MITCHELL: No, I'm good.

23 MR. PLATT: Okay. So, in the *Vizio* case, the Board initially
24 determined that an independent claim was not invalid because of what was
25 referred to as a failed mapping for a given limitation. However, in analyzing

1 the dependent claim, the Petitioner addressed that problematic limitation
2 mapping.

3 Now, because the Board found that the dependent claim is obvious
4 with that analysis, the Board also concluded that the independent claim was
5 obvious. And in fact, the patent owner actually requested Director Review
6 on that, and that was denied, and that's in Paper 38.

7 And the Review Panel noted that, in considering the content of
8 Petitioner's Claim 6 obviousness analysis, the original Panel noted that
9 analysis is being an additional way to evaluate obviousness for Claim 1. We
10 are unpersuaded that, in doing so, the original Panel went beyond the
11 theories presented in the Petition to determine that Claim 1 would have been
12 obvious.

13 So we think that's something the Board should take into account with
14 respect to Dependent Claim 17.

15 Another issue that Patent Owner raised was this idea that association
16 cannot be followed by association via polymerization. And this sort of
17 pervades some of their arguments, so it's that you can't have both. And what
18 we have shown in the Petition is that you actually can have association that
19 takes place, and then there can be polymerization that is also association.
20 They aren't mutually exclusive terms.

21 Now, there was also some number of criticisms about, you know, their
22 sort of the nitpicking of the various cartoons that were used to illustrate
23 concepts. They're visual aids to reflect concepts. The combinations here are
24 the prior art references. And this is in a situation where, for example, if you
25 look at some of the figures in the patent where they don't have hatch marks,

1 that there would be some idea that there's no DNA bases there because
2 there's no hatch marks. It's just taken out of context.

3 I would also say, with respect to some of the hybridization arguments
4 that were made, and we saw Patent Owner's expert with all the spaghetti
5 diagrams that were out there. They argue that that -- that is all based on
6 Patent Owner's expert's unfounded concerns. His declaration includes no
7 references supporting these mis-hybridization theories, and that, although he
8 does point to, for example, a couple of references, in terms of from the
9 Kanan reference, those are all related to addressing unintended
10 hybridization. It's just taken out of context, but there's no support for it. It's
11 just a parade of horrors that are sort of made up without a basis.

12 JUDGE CHANG: And so, Counsel, I do want to make sure I confirm
13 one thing. I think Patent Owner said that Petitioner expert -- and I just want
14 to make sure that the Petitioner agrees that the primer sequence for the
15 polymerization is, in Petitioner's position, is identical for all A and B pairs.
16 Is that correct?

17 MR. PLATT: I'm sorry, Your Honor. Could you repeat that?

18 JUDGE CHANG: Sure. The primer sequences for the
19 polymerization, I believe Patent Owner argued that if you have the same
20 sequence for polymerization, for the primer sequence for the polymerization,
21 for each of the A and B, then you would be more likely to have false
22 positives. And I wanted to confirm that it is Petitioner's position that the
23 primer sequences are identical for each of the pool elements, for the A pool
24 and the B pool.

25 MR. PLATT: Yes, I believe that's right, ma'am.

26 JUDGE CHANG: Okay. Thank you.

1 MR. PLATT: And if the Board would indulge us for one minute just
2 to address Grounds 3 and 4?

3 JUDGE MITCHELL: Sure.

4 MR. PLATT: Given the questions?

5 JUDGE MITCHELL: Sure. We can add time to Patent Owner.

6 MS. BENNETT: Thank you, Your Honor. So I'll be very brief. So,
7 first, Petitioner's identification of the molecules of interest in Baez has not
8 been a moving target. In Dr. Nelson's declaration, at Exhibit 1005, at
9 paragraph 276, he states, applying Patent Owner's positions, a POSA would
10 have understood that the antibodies taught in Baez are molecules of interest.

11 If I can, please, have Slide 90, please. Then, briefly, I'd just like to
12 briefly address the selecting and detection steps in Claim 1(d) and Claim
13 1(e).

14 So, in sum, both 1(d) and 1(e) are taught in Baez, because the cis-
15 reactive cells, which are mapped in Baez to the ASAs, were selected in 1(d)
16 with the selection of the ASA via affinity purification, using a biotin linker,
17 and then, the ASAs ligated nucleic acid labels, which includes the two tags
18 of Landegren with an amplified and detected via PCR.

19 So Patent Owner makes this argument that Baez's amplified ASA
20 product would not detect the two nucleic acids, which are the -- include the
21 Landegren tag, but this is just wrong. This is discussed in detail at Exhibit
22 1051, at paragraphs 100 and 105, and it's very clear that the Landegren tags
23 are maintained.

24 So, in short, when the ligation product is detected and analyzed in
25 Claim 1(e), the nucleic acid labels include the two identification sequences,
26 which are the Landegren tags. Thank you for the additional time.

1 JUDGE MITCHELL: Thank you.

2 MR. HOLMAN: I'd just like to make a few points on our rebuttal
3 here. First, I'd like to address Petitioner's allegations that Dr. Pentelute
4 doesn't provide any support for his opinions, that his opinions should get
5 little weight, they argue, because it's based on experts' say-so, I think is the
6 phrase they use.

7 And what we point out is that, or what I'd like to point out, is that
8 Dr. Pentelute explains his positions. He explains in careful detail the
9 rationale and the science behind these problems with cross-hybridization
10 between these structures. Whether it's from the regular, you know,
11 embodiment, where there's allegedly a polymerization step, or it's the
12 embodiment where there is a hybridization -- or excuse me -- a splint
13 oligonucleotide to do the ligation step, Dr. Pentelute explains his opinions in
14 careful detail, with detailed figures throughout, and he does cite evidence,
15 right?

16 So Dr. Pentelute, he cites exhibits, such as Exhibit 2011. That's the
17 Mullis Paper. He cites Exhibit Slide 2012. That's his Sambrook manual.
18 And these references discuss concepts of nucleic acid chemistry,
19 oligonucleotide primers, hybridization, and template nucleic acid principles,
20 all right? Compare that with Dr. Nelson, who doesn't explain himself, right?
21 He says, oh, you'd be motivated to perform polymerization, and he leaves it
22 at that in his opening declaration, okay?

23 So that's the imbalance that we have here. One expert on Patent
24 Owner's side who carefully explains his -- the background and rationale of
25 his opinions, and does provide evidence, and the other expert on the
26 Petitioner's side, who carries the burden of persuasion in this proceeding,

1 who provides conclusory statements and explanations to support his
2 opinions.

3 Second, I'd like to point out, and this is what we have here on Patent
4 Owner's Slide 31, is this, the structure here, which, allegedly, is the selected
5 molecule in Petitioner's revised versions in the reply.

6 And I just want to point out that we explained this earlier that this
7 molecule doesn't have the associated oligonucleotide anymore. There's only
8 one purple region, whereas the alleged cis-reactive cell has two purple
9 regions, so that's the associated oligonucleotide. So we're missing one of the
10 association elements in this structure. Petitioner never disputes that. This is
11 missing. And so, on that, you know, that's one more reason, which we've
12 pointed out, that this structure, which, according to Petitioner, this is after
13 selection, but before detection Step E, this structure is not a cis-reactive cell.

14 On the plain and ordinary meaning, Petitioner argues, you know,
15 alleged that, well, the issue is whether the selecting step should be limited to
16 affinity capture, but that's not -- that's not really the issue. The issue is how
17 Petitioner presented it in the Petitioner -- the Petition. Excuse me.

18 What did the Petitioner rely on? If you turn to Patent Owner's Slide
19 12, just as a reminder, this is -- this was the petition's argument for Claim 1,
20 Step D, all right? We -- Patent Owner didn't limit it to affinity interaction or
21 biotin affinity selection. Petitioner did. Petitioner explicitly, exclusively
22 pointed to this as teaching Claim Element 1(d), and that's the problem of
23 Petitioner's own creating. We didn't limit it. Patent Owner didn't limit it.
24 Petitioner did.

25 We've heard a lot of explanation today from Counsel for Petitioners
26 about how this process would work and how polymerization would work,

1 and it would copy over the barcodes or the identification sequence elements
2 to create a double-coding code, and lots of detail and explanations in how,
3 how this is all allegedly, you know, described and presented in the petition.

4 But if you turn to Patent Owner's Slide 37, just as a reminder, this is,
5 you know, this is an example of the Petitioner's conclusory arguments. And
6 conclusory statements like this, where they wave their hands and say, oh,
7 polymerization would have been obvious, that's not enough to support a
8 finding of obviousness. That's *In re Van Os*, 844 F.3d 1359, at 1361, and
9 that's *Personal Web v. Apple*, 848 F.3d 987, at 994.

10 And one more point on Petitioner's figures I'd like to point out. If you
11 could, turn to Patent Owner's Slide 29. And Petitioner says we are
12 nitpicking the changes and revisions to the figures, and it's all there, and
13 we're just quibbling over just minor details. But this is just an example of
14 what, in Petitioner's reply, what they point to as allegedly supporting these
15 new figures, right?

16 And according to Petitioner, the support for these revised figures
17 spans over 14 different pages of the petition, 9 different paragraphs from its
18 expert declaration, and four different pages of deposition testimony, and you
19 have compile -- cobble all that together to come up with these revised
20 figures that are now presented in the reply.

21 And so, we've explained this in our Sur-reply, neither the Board nor
22 Patent Owner should be forced to play archeologist in the record and have to
23 sort through all this to figure it all out. That's *Parus Holdings v. Google*, 70
24 F.4th 1365, at 1372.

25 Now, if you could, turn to Patent Owner's Slide 60, please. This is
26 related to Petitioner's Ground 3. Petitioner says that the arguments for

1 Ground 3 are not a moving target, that they've labeled, that they've claim
2 mapped consistent with what Patent Owner has said or mapped in district
3 court. But you'll see here, this is -- this is the example that we've, you know,
4 presented in our Patent Owner's Sur-reply, and the Board noticed this, too, at
5 its decision on Institution. That is a moving target, right?

6 So, in the petition, the Petition argues that the MOIs, including -- this
7 is on the left, the top box there -- Petition points to Baez's antibody-nucleic
8 acid conjugates and says, the MOIs include Baez's antibody-nucleic acid
9 conjugates. And then, in the next breath, on Page 56, they point to the same
10 thing in Baez, these reported conjugates, and they say, oh, the interactors
11 include Baez's reporter conjugates. So they point to the same -- two
12 different -- excuse me -- the same disclosure in Baez as meeting 2 different
13 elements of the claims. And the Board noticed this. There is -- that's
14 inconsistent, right?

15 And this inconsistency is not -- isn't resolved in the reply. In the
16 reply, they said, oh, we're mapping it the same as Patent Owner did in
17 district court. If we turn to Slide 61, we have an example of this language
18 here.

19 And the Petitioner is mischaracterizing what we've argued in district
20 court. In district court, you can see Patent Owner mapped -- just states that
21 the matched antibody pairs in the NULISA product, by the way, not -- this is
22 not discussing Baez -- the antibody pairs in NULISA are molecules of
23 interest, and the antibody and nucleic acid, together, form the interactors,
24 right? So, Patent Owner is not being inconsistent. It's Petitioner who is
25 inconsistent. And this doesn't justify Petitioner's inconsistent claim mapping
26 in the -- in Grounds 3 and 4.

1 Finally, I'd like to make a quick point on Claim Element 1(e) in
2 Grounds 3 and 4. This is if you turn to Patent Owner's Slide 68, please. So,
3 here, as we've explained in our Patent Owner's Response and the surreply,
4 the Petitioner fails to show that this art combination teaches Step E for two
5 reasons.

6 Again, similar to Grounds 1 and 2, because the art doesn't teach or
7 suggest practicing Step D, selecting all cis-reactive cells, it likewise doesn't
8 teach or suggest practicing Step E, which requires subjecting the associated
9 oligonucleotides from the cis-reactive cells that were selected. So that's part
10 one.

11 And part two, as we explain in our Patent Owner's Response and Sur-
12 reply, is that for the detection step, Petitioner only relies on detecting a
13 ligation product when they're discussing Claim 1. For example, this is in
14 Patent Owner's Slide 69, Petition points to amplifying ASA with PAC --
15 PCR and subsequent detection, as taught in Baez.

16 If you look at Baez, Baez, the detection that Baez discloses is running
17 a PCR amplicon on a gel and looking at is there a band there or not. The
18 Petitioner doesn't explain how detecting a ligation product is detecting the
19 two alleged identification sequence elements that come from the Landegren
20 reference. It's, you know, there's a ligation product there; yes or no? Are the
21 identification sequence elements there? That's what Petitioner doesn't
22 explain when addressing Claim 1.

23 All right. In closing, Petitioner has failed to make its case in the
24 Petition to institute. That's required by the statute, by this Board's
25 guidelines, and by legal precedent. That's *Intelligent Bio-Systems v.*
26 *Illumina*, 1359. That's *Wasica Finance v. Continental Auto*, at 1286. That's

1 *Henny Penny v. Frymaster*, at 1331, and that's *Personal Web v. Apple*, at
2 994. Long line of case law precluding Petitioner from changing its
3 arguments the way it has in this case.

4 But even if you look at the merits of this case, Your Honors,
5 Petitioner still hasn't met its burden of persuasion here. The Petition fails to
6 show that Kanan, Neri, and Famulok teach or suggest all the elements of the
7 challenged claims in Grounds 1 and 2. And likewise, the Petition fails to
8 show that Baez, Landegren, and Freskgard teach or suggest all the elements
9 of the challenged claims in Grounds 3 and 4.

10 Now, this is a fundamental requirement, not only under the law for
11 obviousness, but also under the Board's rules, right? You can look at Rule
12 104(b)(4), which states, quote, the Petition must specify where each element
13 of the claim is found in the prior art, patents, or printed publications relied
14 upon. All right? And there's an abject failure to satisfy that rule in the
15 Petition here.

16 Again, it's Petitioner who carries the burden of persuasion throughout
17 this entire trial, and Petitioner has failed to meet its burden in this case.
18 Thank you.

19 JUDGE CHANG: Counsel, let me ask one really quick question.
20 Hopefully, there's still a little time. So, on page 43, if you look at page 43 of
21 your demonstratives, you have a figure of Dr. Pentelute saying that it's likely
22 that there will be false negatives and false positives presented.

23 I guess my question is, if you look at, for example, the picture on the
24 right, where you have two B pool molecules bound to two separate
25 hybridization areas, and I think Petitioner's argument is going to be this is
26 not -- there are ways to deal with this. For example, the one of the B pool

1 molecules is going to be already be close to the A pool molecule because of
2 the first hybridization. So, how likely is it that actually both of these two
3 different molecules would bind to the same A molecule, and did
4 Dr. Pentelute address that?

5 MR. HOLMAN: Well, so --
6 (Simultaneous speaking.)

7 MR. HOLMAN: I'm sorry.

8 JUDGE CHANG: Go ahead.

9 MR. HOLMAN: I didn't mean to cut you off.

10 JUDGE CHANG: No, that's it, that just, basically, it's possible, but
11 did he address how likely it is to happen?

12 MR. HOLMAN: Well, I don't know if he provided a percentage of
13 odds of this happening, Your Honors. But the, you know, based on the basic
14 principles of nucleic acid chemistry and hybridization, is what he's pointing
15 out is that, if you mix these together in this soup, they're going to -- and
16 they're under, you know, appropriate hybridization conditions, you're going
17 to get this cross-hybridization effect.

18 And Petitioner points to, you know, disclosures in the Kanan
19 reference, and says, oh, well, Kanan didn't have any issues with cross-
20 hybridization. They say Neri didn't have any issues with cross-
21 hybridization. But if you look at those references, those are not set up the
22 way the Petitioner has with these multiple universal hybridization sequences.

23 And even Neri, which they rely on Example 3 in the Neri reference,
24 that's a prophetic example. And there's only two oligonucleotides in the
25 entire system, and they can only hybridize with each other in one spot. So,
26 of course, there's no unintended hybridization there.

1 And just, you know, the burden is on the Petitioner here. They're the
2 ones that need to explain this, that it's not going to be an issue, and how and
3 why. And even in reply, they still don't. They just say a POSA could figure
4 it out. And that's our point, is that that doesn't satisfy Petitioner's burden
5 here.

6 JUDGE CHANG: Okay. Thank you.

7 MR. HOLMAN: Thank you.

8 JUDGE MITCHELL: Well, thank you all. And as always, we love
9 oral argument because it lets us ask our questions, and we really appreciate
10 it. It's very, very helpful today. After we adjourn, if you all would remain
11 and just make sure the court reporter doesn't have any questions and
12 spellings on what you said. So, with that --

13 (Whereupon, the above-entitled matter went off the record at 3:10
14 p.m.)

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