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Paper 10
Entered: April 27, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

OXFORD NANOPORE TECHNOLOGIES LTD.,
Petitioner,

v.

UNIVERSITY OF WASHINGTON and
UAB RESEARCH FOUNDATION,
Patent Owner.

Case IPR2015-00057
Patent 8,673,550 B2

Before FRANCISCO C. PRATS, JACQUELINE WRIGHT BONILLA, and SHERIDAN K. SNEDDEN, *Administrative Patent Judges.*

PRATS, *Administrative Patent Judge*.

DECISION
Granting Petitioner's Motion for Joinder
and Instituting *Inter Partes* Review
37 C.F.R. §§ 42.108, 42.122

I. INTRODUCTION

A. Statement of the Case

On October 13, 2014, Oxford Nanopore Technologies Ltd. ("Petitioner") filed a Petition (Paper 1, "Pet.") requesting *inter partes* review of claims 1, 5, 6, 10–12, 16–19, 23, 25, 29, 30, 34, 37, and 41 of U.S. Patent No. 8,673,550 B2 (Ex. 1001, "the '550 patent"). On the same day, Petitioner also filed a Motion for Joinder (Paper 3, "Joinder Motion"), requesting joinder of the Petition with another instituted proceeding, *Oxford Nanopore Techs. v. University of Washington*, Case IPR2014-00513 ("the '513 proceeding"), also involving challenges to claims of the '550 patent. Petitioner filed its Joinder Motion within one month of the September 15, 2014, institution date of the '513 proceeding, as required by 37 C.F.R. § 42.122(b).

The University of Washington and UAB Research Foundation (collectively, "Patent Owner") filed an Opposition to Petitioner's Motion for Joinder (Paper 7, "Opp. to Joinder"), and Petitioner filed a Reply to the Opposition to Motion for Joinder (Paper 8, "Reply to Opp. to Joinder"). Thereafter, Patent Owner filed a Preliminary Response. Paper 9, "Prelim. Resp."

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may be instituted only if "the information presented in the [Petition and Preliminary Response] . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a).

In its Preliminary Response, Patent Owner states that, in its Motion to Amend in the '513 proceeding, it canceled all challenged claims in the '550 patent, except claims 10, 17, and 18, an action that took place after Petitioner filed its Petition in the current case. Prelim. Resp. 4. Therefore, Patent Owner contends, "the only claims left for consideration in the present proceeding are claims 10, 17, and 18." *Id.* We agree and, accordingly, consider Petitioner's challenges only as to claims 10, 17, and 18 in the instant case.

Upon consideration of the instant Petition, we conclude that Petitioner has established a reasonable likelihood that it would prevail in its challenge to claim 10 of the '550 patent, but not as to claims 17 and 18. We, therefore, institute an *inter partes* review as to claim 10. For the reasons discussed below, we also grant Petitioner's Joinder Motion.

B. Related Proceedings

Concurrently with the Petition filed in the '513 proceeding, Petitioner filed another Petition ("the '512 Petition") advancing additional challenges to the claims of the '550 patent. *Oxford Nanopore Techs. v. University of Washington*, Case IPR2014-00512, Paper 1 ("the '512 proceeding"). The Board declined to institute trial on any of the grounds presented in the '512 Petition. *Oxford Nanopore Techs. v. University of Washington*, Case IPR2014-00512, slip op. 20–21 (PTAB Sept. 15, 2014).

C. Proposed Grounds of Unpatentability

Petitioner contends that claims 10, 17, and 18 are unpatentable under 35 U.S.C. § 103(a) based on the following specific grounds (Pet. 6)[1]:

Reference[s]	**Claim[s] challenged**
The '782 patent[2] in view of the Gundlach Grant Abstract[3] or Butler[4]	10
The '782 patent in view of the Gundlach Grant Abstract	17 and 18

D. The '550 patent

The '550 patent discloses using a "*Mycobacterium smegmatis* porin (Msp)" to detect analytes in liquid media. Ex. 1001, 7:54–8:55. The '550 patent explains that a porin is a tunnel-forming multimeric protein through which nutrients pass in mycobacteria. *Id.* at 7:53–55, 18:32–57. Wild-type *M. smegmatis* porins include MspA, MspB, MspC, and MspD. *Id.* at 18:59–

[1] Petitioner supports its challenges with Declarations by James Willcocks, Ph.D. ("Willcocks Decl.") (Ex. 1009), Daniel Branton, Ph.D. ("Branton Decl.") (Ex. 1012), and Dr. Roland Benz ("Benz Decl.") (Ex. 1013).

[2] George Church et al., U.S. Patent No. 5,795,782 (issued Aug. 18, 1998) (Ex. 1006).

[3] Abstract of Gundlach, J, *Engineering MspA for Nanopore Sequencing*, NHGRI Grant Application, No. 1R21HG004145-01, awarded September 25, 2006 (Ex. 1005).

[4] Thomas Butler, *Nanopore Analysis of Nucleic Acids* (2007) (Ph.D. dissertation, Univ. of Washington, Seattle, Washington) (Ex. 1003).

61. The ’550 patent discloses that wild-type or mutant Msp porins may be used in its analytical methods. *Id.* at 7:60–64.

The ’550 patent discloses that the tunnel of an Msp porin includes two sections, a “vestibule,” and a “constriction zone.” *Id.* at 27:15–16.

The ’550 patent states that a “‘vestibule’ refers to the cone-shaped portion of the interior of an Msp porin whose diameter generally decreases from one end to the other along a central axis, where the narrowest portion of the vestibule is connected to the constriction zone. A vestibule may also be referred to as a ‘goblet.’” *Id.* at 27:9–14; *see also id.* at Fig. 1 (showing structure of wild-type MspA porin).

A “‘constriction zone’ refers to the narrowest portion of the tunnel of an Msp porin, in terms of diameter, that is connected to the vestibule.” *Id.* at 27:35–37.

As to its analytical methods, the ’550 patent explains that, when an Msp porin is placed in a lipid bilayer that separates first and second conductive liquid media, application of an electrical field can cause an analyte to be driven into, and/or through, the porin. *Id.* at 7:53–8:16. The ’550 patent explains further:

> The electric field moves an analyte such that it interacts with the tunnel. By “interacts,” it is meant that the analyte moves into and, optionally, through the tunnel, where “through the Msp tunnel” (or “translocates”) means to enter one side of the tunnel and move to and out of the other side of the tunnel.

Id. at 28:1–6.

The analyte may be detected by “measuring an ion current as the analyte interacts with an Msp porin tunnel to provide a current pattern, wherein the appearance of a blockade in the current pattern indicates the

presence of the analyte." *Id.* at 8:13–16. Thus, a "'blockade' is evidenced by a change in ion current that is clearly distinguishable from noise fluctuations and is usually associated with the presence of an analyte molecule at the pore's central opening." *Id.* at 33:38–41. "More particularly, a 'blockade' refers to an interval where the ionic current drops below a threshold of about 5–100% of the unblocked current level, remains there for at least 1.0 μs, and returns spontaneously to the unblocked level." *Id.* at 33:43–46.

The '550 patent discloses that "an analyte may be a nucleotide, a nucleic acid, an amino acid, a peptide, a protein, a polymer, a drug, an ion, a pollutant, a nanoscopic object, or a biological warfare agent. Optionally, an analyte is a polymer, such as a protein, a peptide, or a nucleic acid." *Id.* at 8:45–49.

The '550 patent discloses that the negatively charged amino acids in the tunnel of the wild-type MspA are thought to inhibit DNA entry into the porin. *Id.* at 42:15–19. Thus, the '550 patent describes embodiments in which negative amino acids in the constriction zone, vestibule, and around the entrance of wild-type MspA are replaced with positively charged residues, so as to allow more optimal translocation of single-stranded DNA through the porin. *Id.* at 42:19–22, 45:45–46:13.

Claims 1, 10, 17, and 18, recite the challenged subject matter under consideration herein, and read as follows:

1. A method for detecting the presence of an analyte, comprising:

applying an electric field sufficient to translocate an analyte from a first conductive liquid medium to a second conductive liquid medium in liquid communication through a *Mycobacterium smegmatis* porin (Msp) having a vestibule and a constriction zone that define a tunnel; and

measuring an ion current, wherein a 5% or more reduction in the ion current for at least 1.0 μs compared to an ion current level for the Msp without an analyte present indicates the presence of the analyte in the first medium.

10. The method of claim 1**,** wherein at least one of the first or second conductive liquid media comprises a plurality of different analytes.

17. A system comprising a *Mycobacterium smegmatis* porin (Msp) having a vestibule and a constriction zone that define a tunnel,

wherein the tunnel is positioned between a first conductive liquid medium and a second conductive liquid medium allowing liquid communication between the first and second conductive liquid media,

wherein at least one conductive liquid medium comprises an analyte, and

> wherein the system is operative to detect the analyte when the system is subjected to an electric field sufficient to translocate the analyte from one conductive liquid medium to the other.
>
> 18. The system of claim 17, wherein the Msp is a mutant comprising at least a first mutant MspA monomer.

II. ANALYSIS

A. Claim Construction

The Board interprets claims in an unexpired patent using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 778 F.3d 1271, 1278–81 (Fed. Cir. 2015). Under that standard, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech. Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

Petitioner "submits that no terms, other than those already construed by the Board in connection with IPR2014-00513, are in need of construction." Pet. 20. Patent Owner does not contend otherwise, nor does Patent Owner proffer any specific construction of any claim terms.

In the '513 proceeding we noted that claim 1 of the '550 patent requires "applying an electric field sufficient to translocate an analyte from a first conductive liquid medium to a second conductive liquid medium in liquid communication through a *Mycobacterium smegmatis* porin (Msp) having a vestibule and a constriction zone that define a tunnel." *Oxford*

Nanopore Techs. v. University of Washington, Case IPR2014-00513, slip op. 8 (PTAB Sept. 15, 2014) (citing Ex. 1001, 103:35–39, 105:22–23).

Given its express language, we construed claim 1 as requiring that an analyte, if present, must translocate, that is, move, from the first medium through the Msp porin to the second medium, when the electric field is applied. *Id.* at 9. We apply that construction herein.

B. Obviousness of claim 10 over the'782 patent and Butler

1. The '782 patent (Ex. 1006)

The '782 patent discloses a method for evaluating polymer molecules, such as DNA or RNA, in which "[t]wo separate pools of liquid-containing medium and an interface between the pools are provided. The interface between the pools is capable of interacting sequentially with the individual monomer residues of a single polymer present in one of the pools." Ex. 1006, 1:42–47. The '782 patent discloses that the pools may contain electrically conductive media which are "separated by an impermeable barrier containing an ion permeable passage, and measurements of the interface characteristics include establishing an electrical potential between the two pools such that ionic current can flow across the ion permeable passage." *Id.* at 2:37–42.

The '782 patent explains that "[w]hen the polymer interacts sequentially with the interface at the ion permeable passage, the ionic conductance of the passage will change (e.g., decrease or increase) as each monomer interacts, thus indicating characteristics of the monomers (e.g., size, identity) and/or the polymer as a whole (e.g., size)." *Id.* at 2:42–47. The '782 patent explains further that "[s]everal individual polymers, e.g., in a heterogenous [sic] mixture, can be characterized or evaluated in rapid

succession, one polymer at a time, leading to characterization of the polymers in the mixture." *Id.* at 1:51–54.

> Thus, as to DNA or RNA, the method of the '782 patent involves measurements of ionic current modulation as the monomers (e.g., nucleotides) of a linear polymer (e.g., nucleic acid molecule) pass through or across a channel in an artificial membrane. During polymer passage through or across the channel, ionic currents are reduced in a manner that reflects the properties of the polymer (length, concentration of polymers in solution, etc.) and the identities of the monomers.

Id. at 6:52–59. The '782 patent explains that sequential determination of the identities of the individual nucleotides in the nucleic acid molecules offers a number of advantages in nucleic acid sequencing, including "reduction in the number of sequencing steps, and increasing the speed of sequencing and the length of molecule capable of being sequenced." *Id.* at 5:38–40.

The '782 patent discloses that ion permeable passages useful in its invention include "naturally occurring, recombinant, or mutant proteins which permit the passage of ions under conditions where ions are present in the medium contacting the channel or pore. Synthetic pores are also included in the definition." *Id.* at 3:15–18. "Preferred channels for use in the invention include the α-hemolysin toxin from *S. aureus* and maltoporin channels." *Id.* at 4:65–67. The '782 patent discloses, however, that "[a]ny channel protein which has the characteristics useful in the invention (e.g., minimum pore size around 2 Å, maximum around 9 nm; conducts current) may be employed." *Id.* at 10:13–16.

In Example 5 of the '782 patent, α-hemolysin from *S. aureus* was used to form a current-conducting channel in a lipid bilayer separating two

pools of electrically conductive media. *Id.* at 19:12–25. When a voltage was applied across the membrane, poly A, poly C, and poly U molecules in the media caused transient measurable current blockades consisting of "85–90% reductions of current amplitude [which] lasted up to several milliseconds." *Id.* at 19:44–46.

2. Butler (Ex. 1003)

Butler discloses that nanopore analysis of nucleic acids "has the potential to be a central component of a fundamentally new DNA sequencing methodology." Ex. 1003, 5.[5] Like the '782 patent, Butler explains that nanopore nucleic acid analysis involves placing a current-conducting channel, such as the α-hemolysin protein from *S. aureus*, in a lipid bilayer separating two pools of electrically conductive media, and applying a voltage across the membrane. *Id.* at 15–17. Also, like the '782 patent, Butler explains that the voltage drives the negatively charged DNA through the channel, which is observed as a transient blockade of the ionic current of the system, the measured reduction in current allowing detection of the DNA. *Id.*

Butler discloses results from a "collaborative research effort . . . to engineer a porin ('MspA') found in the outer membrane of *Mycobacterium smegmatis* for application in nanopore analysis of nucleic acids." *Id.* at 88. Butler discloses that the MspA porin "has many advantageous characteristics for nucleic acid analysis including a short, narrow inner constriction,

[5] In citing to Butler, we cite to the page numbers inserted at the bottom right corner of each of the pages of Exhibit 1003.

remarkable robustness, ease of use, and the retention of pore-forming activity despite the introduction of multiple amino-acid substitutions." *Id.*

Butler found initially, however, that the wild-type MspA porin did not interact with single-stranded DNA molecules (ssDNA). *Id.* Nonetheless, "a mutant with all of the excess negative charge removed has recently demonstrated frequent transient current blockades in the presence of ssDNA. We are presently working to verify the exciting possibility that these blockades are a result of interaction between ssDNA and the MspA mutant." *Id.*

In particular, Butler describes experiments in which the MspA triple mutant D90S/D91S/D93N ("SSNMspA") provided data "consistent with the scenario where $d\text{A}_{50}$ [ssDNA] molecules are electrophoretically driven into the SSN-MspA pore and cause transient blockades of the ionic current." *Id.* at 107. Despite these results, Butler discloses:

> While this $d\text{A}_{50}$-induced blockade explanation is both plausible and encouraging, we can identify at least two other candidate mechanisms for the observed blockade rate increase. First, it is possible and even likely that MspA gating can be induced by molecules other than single-stranded nucleic acids. For example, gating in α-HL can be induced by a variety of divalent and trivalent cations. Such molecules would be contaminants in our DNA experiments. . . . A second possibility is that the moderate rate of transient blockades observed in the DNA-free control experiments results from intrinsic conformational fluctuations of the SSN-MspA structure.

Id. (citation omitted).

Accordingly, Butler discloses, "[i]t will be necessary to obtain direct proof of translocation by directly detecting single-stranded DNA molecules

on the *trans* side of the bilayer after an experiment." *Id.* at 110 (citations omitted). Butler discloses, moreover, that even if the blockades exhibited by the SSN-MspA mutant "are not caused by translocation of dA_{50}, there are still a number of reasonable mutation strategies to pursue in our effort to engineer another protein pore that allows DNA translocation." *Id.* at 111. Butler discloses, that if the "milestone" of DNA translocation is achieved,

> then we will begin a series of comparative experiments with a variety of mutants with the dual goals of optimizing MspA for nucleic acid analysis and understanding the nanoscale mechanisms that govern electrophoretic translocation of ssDNA and RNA through MspA. Results from these experiments will give significant insight into the physics underlying nanopore analysis and will hopefully lead to new MspA-based nanopore biosensors with improved analytical capabilities.

Id.

3. Analysis

Petitioner presents a claim chart to show where the features required by claim 1, from which claim 10 depends, may be found in the '782 patent and Butler. Pet. 32–37. As to claim 10's requirement that at least one of the two conductive media comprises a plurality of different analytes, Petitioner directs us (*id.* at 38) to column 1, lines 50–54, of the '782 patent, which, as noted above, states that "[s]everal individual polymers, e.g., in a heterogenous [sic] mixture, can be characterized or evaluated in rapid succession, one polymer at a time, leading to characterization of the polymers in the mixture." Ex. 1006, 1:51–54.

Petitioner contends that the '782 patent describes methods having all of the steps and features of claim 10, except the use of an Msp porin. *See* Pet. 24, 38–39. Petitioner contends that an ordinary artisan would have been

motivated to modify the '782 patent's methods to incorporate Butler's mutant MspA porin, given the references' expressed common goals of using a nanopore to effect rapid nucleic acid analysis. *Id.* at 24–25. In particular, Petitioner contends that an ordinary artisan would have considered the use of Butler's MspA mutant porin in the methods of the '782 patent to be "nothing more than the predictable use of a prior art element according to its established function." *Id.* at 29, 31.

Petitioner persuades us, on the current record, that an ordinary artisan would have been prompted to use Butler's mutant MspA porin as the channel protein in the nucleic acid analysis methods described in the '782 patent.

As Petitioner discusses (Pet. 26), and as noted above, the '782 patent discloses that any channel protein having appropriate properties may be used in its methods. Ex. 1006, 10:13–15. As Petitioner discusses (Pet. 29), and as noted above, Butler discloses that its "SSN-MspA" mutant exhibited properties consistent with the translocation of ssDNA through the protein's pore, using essentially the same system as that described in the '782 patent. Ex. 1003, 107. As Petitioner discusses (Pet. 26–27), and as noted above, Butler discloses that the MspA porin, in general, has a number of advantageous properties, including a short, narrow inner constriction, significant robustness, and ease of use. Ex. 1003, 88.

Given Butler's disclosure that its SSN-MspA mutant porin exhibited properties consistent with the DNA translocation required in the methods of the '782 patent, and given also the advantageous properties of MspA porins disclosed by Butler, Petitioner persuades us, on the current record, that an ordinary artisan would have been prompted to use Butler's SSN-MspA

mutant porin in the '782 patent's nanopore-based nucleic acid analysis methods. On the current record, Patent Owner's arguments do not persuade us to the contrary.

Patent Owner contends that Butler expressed skepticism as to whether its results involved DNA translocation, and that Butler cautioned that mechanisms other than translocation may have been responsible for the results of its experiments. Prelim. Resp. 23–25. Thus, Patent Owner contends, an ordinary artisan "reading Butler's cautionary statements regarding the inconclusiveness of his single-analyte experiments with respect to translocation would have had no reasonable expectation that the method could successfully be used with multiple analytes, as claim 10 requires." *Id.* at 25. Patent Owner contends that Petitioner offered no evidence to the contrary, and failed to address this issue entirely. *Id.*

On this record, Patent Owner's arguments do not persuade us that Petitioner has failed to provide a necessary showing for us to institute a trial on this ground.

We acknowledge Butler's recognition that the experimental results suggesting ssDNA translocation by the SSN-MspA protein may have been due to factors unrelated to translocation, and that translocation therefore required further verification. *See* Ex. 1003, 88, 107, 110–11. It is well-settled, however, that "[o]bviousness does not require absolute predictability of success. . . . For obviousness under § 103, all that is required is a reasonable expectation of success." *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009) (quoting *In re O'Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988) (emphasis removed).

As the Federal Circuit explained in *Kubin*, one circumstance in which the prior art fails to provide a reasonable expectation of success is where the art suggests "vary[ing] all parameters or try[ing] each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." *Id.* at 1359 (quoting *O'Farrell*, 853 F.2d at 903).

Another circumstance in which the prior art fails to provide a reasonable expectation of success is where the art suggests exploring a "general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *Id.*

In the instant case, as noted above, Butler describes a single specific protein, SSN-MspA, with a specific amino acid sequence, that exhibits properties consistent with those required by the '782 patent in its nanopore-based nucleic acid analytical methods. Thus, rather than requiring the ordinary artisan to vary numerous parameters, select from numerous choices, or apply a promising but unguided general approach, the artisan need only have substituted the SSN-MspA porin for the nanopores described in the '782 patent. That is, on the current record, given the teachings in the prior art advanced by Petitioner, an ordinary artisan need only have used Butler's protein in the '782 patent's methods to verify its suitability in those methods. Accordingly, on the current record, Petitioner persuades us that '550 patent simply confirmed the suitability, already suggested by Butler, of SSN-MspA in nanopore-based nucleic acid analysis.

We, therefore, determine that, on this record, Petitioner has shown a reasonable likelihood of prevailing in its obviousness challenge to claim 10 of the '550 patent, based on the '782 patent and Butler.

C. Obviousness of claims 10, 17, and 18 over the'782 patent and the Gundlach Grant Abstract

1. Gundlach Grant Abstract (Ex. 1005)

The Gundlach Grant Abstract discloses that the "electrophoretic passage of single-strand DNA through a nanopore has the potential to become an inexpensive, ultrafast DNA sequencing technique." Ex. 1005, 1. The Gundlach Grant Abstract states that its investigation "propose[s] to develop the Mycobacterium smegmatis porin A (MspA) into a new pore for nanopore sequencing." *Id.* The Gundlach Grant Abstract discloses:

> MspA is a promising platform for engineering a nanopore sequencing device for a number of reasons: (i) Its short, narrow constriction zone may give it higher sequencing sensitivity and resolution. (ii) MspA is extremely robust (iii) Formation of stable MspA pores is easy and reliable. (iv) A wide range of stable MspA mutants can be readily engineered.

Id.

The Gundlach Grant Abstract discloses, however, that

> [i]n preliminary studies neither wild-type MspA nor MspA with a mutation in its constriction zone allowed translocation of DNA. Therefore, our goal is to tailor MspA for efficient translocation of DNA. We will remove excess negative charges from the rim and vestibule of the pore by site-directed mutagenesis, stabilize the loops near the constriction zone, and optimize the constriction zone for DNA passage. Translocation will be tested with a variety of ssDNA constructs in conditions designed to facilitate translocation. Once translocation is realized, further experiments will inform subsequent mutations to optimize MspA for nanopore sequencing.

Id.

Analysis

Petitioner cites the '782 patent as describing systems and methods having all of the features of claims 10, 17, and 18 of the '550 patent, except the use of the *Mycobacterium smegmatis* porin required by the challenged claims. Pet. 24, 45. Petitioner contends that an ordinary artisan would have been motivated to modify the '782 patent's methods to incorporate a mutant MspA porin, such as that disclosed in the Gundlach Grant Abstract, given the references' expressed common goals of using a nanopore to effect rapid nucleic acid analysis. *Id.* at 24–25. In particular, Petitioner contends that an ordinary artisan would have considered the use of the Gundlach Grant Abstract's MspA mutant porin in the methods of the '782 patent "nothing more than the predictable use of a prior art element according to its established function." *Id.* at 29, 31, 46, 47.

We agree with Patent Owner (*see* Prelim. Resp. 20–23) that Petitioner has not established a reasonable likelihood of prevailing in its obviousness challenge to claims 10, 17, and 18 of the '550 patent, based on the '782 patent and the Gundlach Grant Abstract.

We acknowledge the teachings in the Gundlach Grant Abstract, noted above, that MspA porins have qualities that would have made them desirable for use in nanopore-based methods of nucleic acid analysis. Ex. 1005, 1. As noted above, and as Patent Owner points out, however (Prelim. Resp. 20–21), wild-type and mutant MspA porins had not achieved the DNA translocation capacity required in the methods of the '782 patent. *See* Ex. 1005, 1 ("In preliminary studies neither wild-type MspA nor MspA with a

mutation in its constriction zone allowed translocation of DNA."). Indeed, the Gundlach Grant Abstract merely proposes strategies by which a potentially useful porin might be obtained by modifying existing wild-type or mutant MspA porins. *Id.*

Thus, contrary to Petitioner's assertions (Pet. 29, 31, 46, 47), rather than disclosing a specific protein like Butler, discussed above, the Gundlach Grant Abstract does not describe a prior art element having an established function which an ordinary artisan would have simply substituted for the pores used in the '782 patent. To the contrary, the Gundlach Grant Abstract's hopeful disclosure that a porin useful in nucleic acid analysis potentially might be obtained after pursuing different mutation strategies is the type of teaching discussed in *Kubin* as failing to provide a reasonable expectation of success. *Kubin*, 561 F.3d at 1359 (insufficient showing of reasonable expectation of success where prior art suggests exploring a "general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it").

In sum, Petitioner does not persuade us that the Gundlach Grant Abstract describes a prior art element having an established function that an ordinary artisan would have substituted for the pores used in the '782 patent. Accordingly, Petitioner does not persuade us that it has established a reasonable likelihood of prevailing in its obviousness challenge to claims 10, 17, and 18 of the '550 patent, based on the '782 patent and the Gundlach Grant Abstract.

D. Arguments under 35 U.S.C. § 325(d)

Section 325(d) states that, "[i]n determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office." 35 U.S.C. § 325(d)

Patent Owner argues that we should exercise our discretion under § 325(d) and deny the Petition, because granting it effectively provides Petitioner with an improper "second bite at the apple" which attempts to correct the deficiencies in the '512 Petition, but which presents substantially the same references and arguments rejected in the Institution Decision in the '512 proceeding. Prelim. Resp. 1. Patent Owner contends that Petitioner is "not entitled to multiple attempts to 'get it right,' with each successive attempt guided by the Board." *Id.* at 2.

We acknowledge that the Board has, in certain instances, denied second or "follow-on" petitions for *inter partes* review ("IPR") where those second petitions presented substantially the same prior art and arguments presented previously, or presented art and arguments which could have been presented previously, and merely addressed deficiencies in the first petitions noted by the Board. Prelim. Resp. 5–11 (citing *Conopco, Inc. v. The Procter & Gamble Co.*, Case IPR2014-00506, slip op. 4–5 (PTAB December 10, 2014); *Zimmer Holdings, Inc. v. Bonutti Skeletal Innovations LLC,* Case IPR2014-01080, slip op. 4–6 (PTAB October 31, 2014); *CustomPlay, LLC v. ClearPlay, Inc.*, Case IPR 2014-00783, slip op. 5–6 (PTAB November 7, 2014); *Unilever, Inc. v. Procter & Gamble Co*., Case IPR2014-00506, slip op. 6 (PTAB July 7, 2014)).

As Petitioner contends, however, the Board also has declined to deny petitions under § 325(d) in similar circumstances, but where different disclosures were relied upon in previously presented prior art. Pet. 15–16 (citing *Samsung Elecs. Am., Inc. v. LED Tech Devel., LLC*, Case IPR2014-00590, slip op. 8 (PTAB Sept. 3, 2014)).

Ultimately, the decision whether to deny a petition under § 325(d) is discretionary, as Patent Owner recognizes. We acknowledge that Petitioner relied on the '782 patent in the '512 Petition for an improperly incorporated teaching, and that Petitioner also advanced the Gundlach Grant Abstract in the '512 proceeding. *See* Prelim. Resp. 9, 13–14. As noted above, however, we decline, on the merits, to institute trial on grounds based on the Gundlach Grant Abstract. Moreover, as to the challenge to claim 10 based on the '782 patent and Butler, Petitioner has not presented substantially the same arguments as presented in the '512 Petition, as shown by our determination to institute a trial in relation to this ground and claim here, in contrast with our prior decision not to institute a trial based on the '512 Petition.

We are mindful of the significant concerns regarding harassment of patent owners. *See* Prelim. Resp. 10–11. As discussed above, however, the instant case involves only a single additional ground, involving a single claim already under challenge. Moreover, once a Final Decision issues in this proceeding, Petitioner, as well as a real party in interest or privy of the Petitioner, will be estopped from "request[ing] or maintain[ing] a proceeding before the Office with respect to that claim on any ground that the petitioner raised or reasonably could have raised during that inter partes review." 35 U.S.C. § 315(e).

In sum, considering the totality of the circumstances, we decline to exercise our discretion under § 325(d) to deny the Petition.

E. Joinder

The statute governing joinder in *inter partes* review proceedings, 35 U.S.C. § 315(c), reads as follows:

> (c) JOINDER.—If the Director institutes an inter partes review, the Director, in his or her discretion, may join as a party to that inter partes review any person who properly files a petition under section 311 that the Director, after receiving a preliminary response under section 313 or the expiration of the time for filing such a response, determines warrants the institution of an inter partes review under section 314.

Petitioner requests joinder of this proceeding with IPR2014-00513. Joinder Motion 1. Petitioner contends that the Board previously has allowed joinder of additional grounds presented by the same party. *Id.* at 5–7 (citing *Ariosa Diagnostics v. Isis Innovation Limited*, Case IPR2013-00250, slip op. 1 (PTAB Sept. 3, 2013); *Samsung Elecs. Co., Ltd. v. Virginia Innovation Sciences, Inc.*, Case IPR2014-00557, slip op. 8 (PTAB June 13, 2014); *Microsoft Corp. v. Proxyconn, Inc.*, Case IPR2012-00026, slip op. 2 (PTAB Feb. 25, 2013); *Sony Corp. v. Yissum Research Dev. Co. of the Hebrew Univ. of Jerusalem*, Case IPR2013-00327, (PTAB Sept. 24, 2013). Petitioner notes also that the two proceedings for which joinder is requested challenge the same claims of the same patent, and present overlapping prior art. *Id.* at 8.

Patent Owner contends that the Board has held that § 315(c) does not authorize joinder of grounds presented in different petitions by the same party. Opp. to Joinder 4–5 (citing *Target Corp. v. Destination Maternity*

Corp., IPR2014-00508, slip op. 3 (PTAB Sept. 25, 2014). Patent Owner contends that the grounds presented in the two proceedings, anticipation versus obviousness, are sufficiently different such that discovery and briefing will not be simplified. *Id.* at 6. Patent Owner contends further that the schedule of the two proceedings cannot be reconciled without severely curtailing Patent Owner's response and discovery periods. *Id.* at 6–7. Patent Owner contends further that granting joinder here would allow Petitioner to circumvent the rules. *Id.* at 7–8 (citing *Reloaded Games, Inc. v. Parallel Networks LLC*, Case IPR2014-00950, slip op. 3–5 (PTAB October 22, 2014)).

We exercise our discretion to grant joinder in this case. As noted above, Petitioner timely filed its Joinder motion within one month of the institution date of the '513 proceeding, as required by 37 C.F.R. § 42.122(b). The two proceedings involve the same parties, the same claim of the same patent, claim 10, and both cite the Butler reference. Thus, as to claim construction and interpretation of the prior art, the two proceedings involve common issues. As to the decision in *Target*, we note that an expanded panel in that case ultimately held, in a majority decision, that § 315(c) authorizes joinder of additional grounds to a proceeding involving the same parties. *Target Corp. v. Destination Maternity Corp.*, Case IPR2014-00508, slip op. 1–6 (PTAB Feb. 12, 2015).

As to the issue of abuse of the joinder rule to present serial petitions attacking the same claims (Opp. to Joinder 7–8), as Patent Owner acknowledges, there is no copending infringement action involving the claims of the '550 patent. *See* Prelim. Resp. 10–11; Pet. 1. Accordingly, unlike the situation in *Reloaded Games*, grant of the Joinder Motion is not

required to avoid the bar in 35 U.S.C. § 315(b). *See Reloaded Games*, Case IPR2014-00950, slip op. 2 (PTAB Oct. 22, 2014). Specifically, § 315(b) normally bars institution of *inter partes* review when a petition is filed more than one year after the petitioner, its real party in interest, or privy, is served with a complaint alleging infringement of the patent. 35 U.S.C. § 315(b). The one-year time bar, however, does not apply to a request for joinder. *Id*. (second sentence). In the instant case, because neither Petitioner, nor its real party in interest, nor its privy has been served with a complaint alleging infringement of the '550 patent, Petitioner is not using its Joinder Motion as a means to circumvent the § 315(b) bar and obtain consideration on the merits of challenges it otherwise would not be entitled to present.

As to prejudice to Patent Owner resulting from potential scheduling issues, we acknowledge that the '513 proceeding has proceeded to a significant extent, and as such, we herein modify the schedule of the proceeding, as presented in more detail below, to allow Patent Owner a reasonable period to respond to the ground instituted here, and to conduct any associated discovery. Accordingly, Patent Owner does not persuade us that, as a result of this joinder, it will be prejudiced as to the timing of briefing or discovery.

In sum, considering the totality of the circumstances, we exercise our discretion under § 315(c) to grant Petitioner's Joinder Motion to join this proceeding with the '513 proceeding.

III. CONCLUSION

For the foregoing reasons, Petitioner persuades us, on the current record, that it has established a reasonable likelihood of prevailing in its

obviousness challenge to claim 10 of the '550 patent, based on the '782 patent and Butler. As discussed above, however, Petitioner does not persuade us that there is a reasonable likelihood it would prevail in its obviousness challenges to claims 10, 17, and 18, based on the '782 patent and the Gundlach Grant Abstract.

We decline to exercise our discretion to deny the Petition under 35 U.S.C. § 325(d).

We exercise our discretion to grant Petitioner's Joinder Motion to join this proceeding with the '513 proceeding.

IV. CHANGES TO SCHEDULING ORDER

A. Changes to Due Dates

The Scheduling Order entered in IPR2014-00513 (Paper 13), along with any agreed-upon stipulations by the parties to that Scheduling Order in relation to DUE DATES 1, 2, and 3, shall govern the schedule of the joined proceedings with the following exceptions.

The due date, now designated DUE DATE 1A, for Patent Owner to file a supplemental response to the instituted ground in the current Petition, as well as a supplemental motion to amend claim 10 of the '550 patent, in this proceeding is June 29, 2015. Patent Owner's supplemental response shall only address Petitioner's obviousness challenge to claim 10 of the '550 patent as presented in the Petition in IPR2015-00057.

The due date, now designated DUE DATE 2A, for Petitioner to file a supplemental reply to Patent Owner's supplemental response, as well as a supplemental opposition to Patent Owner's supplemental motion to amend, in this proceeding is August 28, 2015.

The due date, now designated DUE DATE 3A, for Patent Owner to

file a reply to Petitioner's supplemental opposition to Patent Owner's supplemental motion to amend, in this proceeding is September 28, 2015.

In the "supplemental" papers due on DUE DATES 1A and 2A, and the reply due on DUE DATE 3A, either party may incorporate by reference portions of the original paper it supplements (e.g., Patent Owner's supplemental response due on DUE DATE 1A may refer to, and incorporate by reference, portions of Patent Owner's Response in IPR2014-00513), but may not incorporate by reference any other paper. The parties may stipulate to a different date for DUE DATES 1A through 5 (earlier or later, but no later than DUE DATE 6, as designated below).

In addition to DUE DATES 1A, 2A, and 3A, revised DUE DATES 4–7 shall apply as designated below:

DUE DATE 1A ..... June 29, 2015

Patent Owner's supplemental response to Petition in IPR2014-00057
Patent Owner's supplemental motion to amend claim 10

DUE DATE 2A ..... August 28, 2015

Petitioner's supplemental reply to supplemental response
Petitioner's supplemental opposition to supplemental motion to amend

DUE DATE 3A ..... September 28, 2015

Patent owner's reply to petitioner's oppositions to motion to amend

DUE DATE 4 ..... ~~May 2, 2015~~ October 19, 2015

Motion for observation regarding cross-examination of reply witness
Motion to exclude evidence
Request for oral argument

DUE DATE 5 ..... ~~May 16, 2015~~
November 2, 2015

Response to observation
Opposition to motion to exclude

DUE DATE 6 ..... ~~May 23, 2015~~
November 9, 2015

Reply to opposition to motion to exclude

DUE DATE 7 ..... ~~June 5, 2015~~
December 3, 2015

Oral argument (if requested)

B. Supplemental Motion to Amend

Notwithstanding the page limits set forth in 37 C.F.R. § 42.24, we hereby expand those limits for the following papers: a supplemental motion to amend, if filed in this proceeding, as well as petitioner's supplemental opposition to the supplemental motion to amend, each are limited to twenty-five (25) pages; Patent Owner's reply to the supplemental opposition to the supplemental motion to amend is limited to twelve (12) pages; and the claim listing may be contained in an appendix to the motion to amend, and does not count toward the page limit of the motion. *See* 37 C.F.R. § 42.5(b).

C. Petitioner's Supplemental Reply

Notwithstanding the page limit set forth in 37 C.F.R. § 42.24(c), Petitioner's supplemental reply to Patent Owner's supplemental response is limited to twenty-five (25) pages. *See* 37 C.F.R. § 42.5(b).

V. ORDER

It is

ORDERED that that Petitioner's Motion for Joinder is granted with respect to the alleged ground, under 35 U.S.C. § 103, that claim 10 of the '550 patent would have been obvious over the '782 patent and Butler;

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(a), *inter partes* review is hereby instituted with respect to the alleged ground, under 35 U.S.C. § 103, that claim 10 of the '550 patent would have been obvious over the '782 patent and Butler;

FURTHER ORDERED that no other ground in the current Petition is authorized for *inter partes* review;

FURTHER ORDERED that this proceeding is joined with IPR2014-00513;

FURTHER ORDERED that changes to the Scheduling Order, as designated above, apply to the joined case, and DUE DATES 1A, 2A, and 3A, and revised DUE DATES 4–7 are set accordingly;

FURTHER ORDERED that that IPR2015-00057 is instituted, joined, and terminated under 37 C.F.R. § 42.72 and all further filings should be made in IPR2014-00513;

FURTHER ORDERED that the case caption in IPR2014-00513 shall be changed to reflect the joinder with this proceeding in accordance with the attached example;

FURTHER ORDERED that because an initial conference call was already held on October 14, 2014, in IPR2014-00513, with which the current proceeding is joined, an initial conference call in the current proceeding is

not necessary. If the parties feel an additional initial conference call with the Board is necessary, they should contact the Board to arrange such a call; and

FURTHER ORDERED that a copy of this Decision be entered into the file of IPR2014-00513.

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

OXFORD NANOPORE TECHNOLOGIES LTD.,
Petitioner,

v.

UNIVERSITY OF WASHINGTON and
UAB RESEARCH FOUNDATION,
Patent Owners.

Case IPR2014-00513[1]
Patent 8,673,550 B2

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[1] Case IPR2015-00057 has been joined with this proceeding.