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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte GREGORY LOHMAN, THOMAS C. EVANS JR.,
and LARRY A. MCREYNOLDS

Appeal 2018-006714
Application 14/839,433
Technology Center 1600

Before JOHN G. NEW, RYAN H. FLAX, and JAMIE T. WISZ,
Administrative Patent Judges.

WISZ, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of ligating DNA polynucleotide sequences. Appellant[1] appeals from the Examiner's decision to reject claims 1–16. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as New England Biolabs, Inc. Appeal Br. 3.

STATEMENT OF THE CASE

The Specification discloses a method "for ligating single stranded polynucleotide fragments, that includes: combining at least two single stranded polynucleotide fragments having complementary regions at a splice junction to an RNA splint and an RNA splint ligase; and permitting the at least two single stranded polynucleotides to ligate to form a single polynucleotide." Spec. 2. The Specification discloses a ligase that "surprisingly ligates ssDNA oligonucleotides splinted by a ssRNA with high efficiency." *Id*. at 12. According to the Specification:

> Contrary to the publication describing PBCV-1 ligase as inactive in ligating DNA oligonucleotides together on an RNA splint (Sriskanda, et al., (1998)), it has here been shown here that ssDNA oligonucleotides of a size greater than 8 nucleotides can surprisingly be ligated together to form a single oligonucleotide of at least 16 nucleotides when splinted by a complementary RNA with an efficiency that is greater than 10 fold to 1000 fold over T4 DNA ligase.

Id. at 13.

Claims 1–16 are on appeal. Claim 1 is illustrative and reads as follows:

> 1. A method for detecting a polymorphism in an RNA, comprising:
>
> (a) hybridizing at least two DNA polynucleotide sequences to a polymorphic sequence in an RNA;
>
> (b) ligating the at least two DNA polynucleotide sequences to one another using a ligase that has an amino acid sequence that is at least 90% identical to the *Chlorella* virus PBCV-1 ligase of SEQ ID NO:1, to produce a ligation product, and

(c) detecting the ligation product of (b), thereby detecting the polymorphic sequence.

Appeal Br. 9 (Claims App'x).

The Examiner rejected claims 1–16 under 35 U.S.C. § 112(a) as failing to comply with the enablement requirement.

ANALYSIS

The Examiner finds that the invention, as claimed, "is not enabled due to problems with the unknown capability of PBCV-1 ligase to ligate DNA utilizing an RNA, lack of specific guidance, and the amount of experimentation required to successfully practice the claimed invention." Final Act. 4. The Examiner acknowledges that the Specification "provides several examples of performing the instant claims," however, the Examiner cites to the prior art reference, Sriskanda[2], as the basis for the enablement rejection. *Id*. at 5–7. The Examiner finds that Sriskanda teaches the ligation steps of the claims and concludes that "PBCV-1 cannot ligate DNA molecules annealed to an RNA template." *Id*. at 5. According to the Examiner, "[t]he instant [S]pecification does not reasonably show that there is a difference between the method steps of Sriskanda [] and the instant claims except in the concentration of DTT." *Id*. at 6.

The Examiner also finds that "[t]here would be a large and prohibitive amount of experimentation required to make and use the claimed invention in the full scope as encompassed by the claims" because "[o]ne would have

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[2] Sriskanda, Verl et al., Specificity and fidelity of strand joining by *Chlorella* virus DNA ligase, Nucleic Acids Research, Vol. 26, No. 15, 3536–3541 (1998) ("Sriskanda").

to determine the difference between the prior art methods and the instantly claimed method to practice the instant claims." *Id*. The Examiner concludes:

> the instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed methods without first making a substantial inventive contribution. As such, claims 1–16 are not enabled, because there would be an undue amount of experimentation required to make and use the invention as claimed and there would be no expectation of success from the prior art.

Id.

Appellant asserts that the Examiner improperly failed to consider their evidence in making the determination that the claims are not enabled. Appeal Br. 4. Specifically, Appellant points to experimental evidence in the Specification that PBCV-1 can efficiently ligate DNA molecules together using an RNA splint. *Id*. at 4–5 (citing Spec. 5:6–7, 5:26–77, 6:8–9, Figs. 2, 4, 5). Appellant also asserts that a post-filing publication by Lohman[3] used the same reagents as described in the present application and showed that PBCV-1 works to ligate DNA substrates under a wide range of conditions and is not sequence specific. *Id*. at 5 (citing Lohman 1832, 1840).

Appellant also contends that the negative results described in Sriskanda are not reproducible, because the Specification repeats the experiments disclosed in Sriskanda, and the method worked. *Id*. at 5 (citing Spec. 6:9–12). Appellant further asserts that Lohman also repeated the

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[3] Lohman, Gregory et al., Efficient DNA ligation in DNA-RNA hybrid helices by Chorella virus DNA ligase, Nucleic Acids Research, Vol. 42, No. 3, 1831–1844 (2013) ("Lohman").

experiments of Sriskanda and found, using an RNA splint, that the oligonucleotides disclosed in Sriskanda were "efficiently ligated under both high and low ATP conditions in 15 min." *Id*. at 5–6 (citing Lohman 1832, 1834). Appellant also cites to several other references as evidence that other groups have shown that PBCV-1 ligase has the ability to ligate DNA molecules that are annealed to an RNA template. *Id*. at 6.

According to the Examiner, Appellant previously argued that one of skill in the art would not look to the method taught by Sriskanda with a reasonable expectation of success because Sriskanda stated that the method did not work. Ans. 7–8 (citing to Feb. 10, 2017 response at 6). Therefore, the Examiner finds that Appellant's "arguments contradict each other because one argument says one of skill in the art would not be motivated to look at the method of Sriskanda and the other argument states one would look to Sriskanda to recreate their methods." *Id*. at 8. The Examiner states that "[t]he reference is either enabled or it is not. If it is not enabled then Applicant's claims are not enabled because they recite the exact elements recited in the method taught by Sriskanda." *Id*.

We find that Appellant has the better position. The Examiner bears the burden of establishing that practicing the full scope of the claimed subject matter would have required undue experimentation. *In re Wright*, 999 F.2d 1557, 156–162 (Fed. Cir. 1993) ("[T]he PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application."). The Examiner's main argument is that the method described in Sriskanda, which uses the same ligation steps as the claimed invention,

was described therein as not working. However, Appellant has provided evidence that the failure described in Sriskanda could not be reproduced. *See* Appeal Br. 5–6. Furthermore, the Specification describes several experimental examples that successfully practice the claimed invention. Spec. 5:6–7, 5:26–77, 6:8–9, Figs. 2, 4, 5. Appellant has also provided post-filing evidence to show that the methods described in the Specification are successful in ligating DNA. *See* Appeal Br. at 5–6.

Although Appellant previously argued that one of skill in the art would not have been motivated to use the method of Sriskanda because it did not work, this argument is not necessarily inconsistent with an argument that the claims, in view of the Specification, are enabled. Sriskanda expressly stated that its method of ligating DNA molecules annealed to an RNA template with PBCV-1 ligase was a failure, thus, the skilled artisan would not consider the reference in seeking to duplicate its method successfully. Here, however, Appellant has presented sufficient evidence to show that the Specification provides guidance to one of skill in the art to practice the claimed method without undue experimentation. Appellant has also presented evidence to show that the failed experiment in Sriskanda could not be reproduced.

Given the disclosure in the Specification and in the references cited by the Appellant, the Examiner does not persuade us that the Specification fails to explain sufficiently to the skilled artisan how to practice the claimed invention. We are not persuaded, therefore, that the Examiner has shown sufficiently that the disclosure in Appellant's Specification fails to enable a skilled artisan to perform the process recited in the claims.

On the record before us, we find that the Examiner erred in rejecting claims 1–16 because of the reasons stated above. Accordingly, we do not sustain the Examiner's enablement rejection of claims 1–16.

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1–16	112(a)	Enablement		1–16

REVERSED