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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DENNIS T. BROWN, RAQUEL HERNANDEZ, MALCOLM E. THOMAS, KATHERINE M. SMITH, and KAVITA NANDA[1]

Appeal 2016-007565
Application 13/069,905
Technology Center 1600

Before FRANCISCO C. PRATS, RICHARD J. SMITH, and JOHN E. SCHNEIDER, *Administrative Patent Judges*.

SCHNEIDER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to modified flavivirus which have been rejected as directed to non-statutory subject matter and as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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[1] Appellants identify the Real Party in Interest as The Research Development Foundation. Appeal Br. 3.

STATEMENT OF THE CASE

"Arthropod vectored viruses (Arboviruses) are viral agents which are transmitted in nature by blood sucking insects." Spec. ¶ 3. Arboviruses include flaviviruses, which cause significant health problems throughout the world. *Id.*

> By their very nature, flaviviruses, like other Arboviruses, must be able to replicate in the tissues of both the invertebrate insect and the mammalian host. Differences in the genetic and biochemical environment of these two host cell systems provide a basis for the production of host range mutant viruses which can replicate in one host but not the other.

Spec. ¶ 4 (citations omitted).

The Specification describes an "engineered nucleic acid comprising a sequence encoding a modified viral transmembrane protein comprising a mutation, wherein the mutation inhibits the production or infectivity of a virus comprising the modified viral transmembrane protein in mammalian cells." Spec. ¶ 7.

Claims 1–10[2] are on appeal. Claim 1 is the sole independent claim and reads as follows:

> 1. A modified flavivirus envelope (E) protein comprising a mutated E protein's N-terminal transmembrane domain (E-T1 domain), such a mutation comprising a deletion of amino acids at positions of 0 to + 3, 0 to +4, -2 to 0, -3 to 0, or -1 to + 1, wherein the unmodified E-T1 domain comprises a central glycine amino acid and the deletion is relative to said central glycine, which is designated as position 0, and wherein the mutation selectively inhibits the replication of a

[2] Claims 11–24 are pending in the application but have been withdrawn from consideration. Final Act. 1.

flavivirus comprising the modified flavivirus E protein in mammalian cells relative to insect cells.

The claims have been rejected[3] as follows:

Claims 1–10 have been rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter.

Claims 1–10 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Hernandez[4] in view of Pugachev[5] and Mukhopadhyay.[6]

NON-STATUTORY SUBJECT MATTER

Issue

The issue with respect to this rejection is whether a preponderance of the evidence supports the Examiner's conclusion that claims 1–10 are directed to non-statutory subject matter.

The Examiner finds that claim 1 reads on a fragment of the naturally occurring protein and that the fragment does not appear to be structurally different from the full-length sequence of the naturally occurring sequence except through cleavage of a peptide bond. Final Act. 3. The Examiner concludes that the claim reads on a product that is not markedly different

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[3] Claims 1–10 were rejected under 35 U.S.C. § 112, first paragraph for failure to comply with the written description requirement. Final Act. 3. The Examiner has withdrawn this rejection. Ans. 2.

[4] Hernandez et al., US 2008/0026004 A1, published Jan. 31, 2008 ("Hernandez").

[5] Pugachev et al., WO 2009/114207 A2, published Sept. 17, 2009 ("Pugachev"),

[6] Mukhopadhyay et al., *A Structural Perspective of the Flavivirus Life Cycle,* 5 Nature Reviews 13 (2005) ("Mukhopadhyay").

from a naturally occurring product and is, therefore, directed to patent ineligible subject matter. *Id.*

Appellants argue that the claimed protein is not a truncated protein but rather a protein with specific internal deletions. Appeal Br. 6. Appellants point out that the claims require that the mutation selectively inhibits the replication of the virus in mammalian cells relative to insect cells. *Id.* Appellants argue that if the protein were truncated as postulated by the Examiner, the virus would not have the ability to infect either type of cells. *Id.* Appellants also argue that the ability to infect and replicate in insect cells while displaying attenuated replication in mammalian cells is a markedly different characteristic as compared to naturally occurring flavivirus. Appeal Br. 7. Finally, Appellants argue that the Examiner has not provided any evidence that a modified flavivirus E protein as described in the claims exists in nature. *Id.*

Analysis

Under § 101, "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof" may be eligible for a patent, subject to the conditions and requirements of the Patent Act. 35 U.S.C. § 101. But, under Supreme Court precedent, "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." *Mayo Collaborative Services v. Prometheus Labs., Inc.*, 566 U.S. 66, 70 (2012) (citation omitted). "Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 591 (2013).

The Supreme Court articulated a two-step test for patent eligibility under § 101 that "distinguish[es] patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014) (citing *Mayo*, 566 U.S. 66) ("the *Alice/Mayo* test"). "First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts. If so, we then ask, what else is there in the claims before us?" *Id.* (citation and quotations omitted). Second, we "search for an inventive concept—i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself." *Id.* (quotations and alterations omitted).

"[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a prima facie case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

We agree with Appellants that the Examiner has failed to establish a prima facie case that the claims are directed to non-statutory subject matter. The Examiner has pointed to nothing in the record nor have we discerned any evidence that that shows that a protein with the specific deletions recited in the claims exists in nature.

The Examiner contends that the claims read on a truncated protein which would include a segment which is the same as what exists in nature. Ans. 3. The Examiner argues that the use of the term "comprises" allows for

additional deletions, which could result in a truncated protein. *Id.* We are not persuaded.

The claims require specific deletions which result in a virus which "selectively inhibits the replication of a flavivirus comprising the modified flavivirus E protein in mammalian cells relative to insect cells." Appeal Br. 17 (Claims App'x). Claim 1 also requires that the modified protein comprise a mutated E proteins N-terminal transmembrane domain. *Id.* We agree with Appellants that these limitations do not encompass truncated proteins. Appeal Br. 6–7; Reply Br. 2. A truncated protein would adversely affect the ability of the virus to infect either insects or mammals and would not contain the N-terminal transmembrane domain. *Id.* Moreover, the Examiner has not offered any evidence that truncated E proteins of flaviviruses exist in nature.

We conclude that a preponderance of the evidence does not support the Examiner's conclusion that the claims are directed to non-statutory subject matter.

OBVIOUSNESS

Issue

The issue with respect to this rejection is whether a preponderance of the evidence supports the Examiner's finding that the subject matter of claims 1–10 would have been obvious over Hernandez combined with Mukhopadhyay and Pugachev.

The Examiner finds that Hernandez discloses genetically engineered membrane enveloped viruses with deletion mutations in the protein transmembrane proteins. Final Act. 8. The Examiner finds that the method

of Hernandez works for any virus that replicates in insects and mammals and contains integral membrane proteins such as flaviviruses. *Id.* The Examiner finds that Hernandez teaches that the deletions can be made in the E1 domain of flaviviruses such as dengue. Final Act. 9.

The Examiner finds that while Hernandez does not teach the central glycine positon of the modified flavivirus protein of the E-T1 domain, this teaching is supplied by Mukhopadhyay, which discloses structural studies of dengue viruses. Final Act. 9–10. The Examiner concludes that "utilizing the teachings of Hernandez and the deletion mutants of Fig. 4, a skilled artisan would easily be able to make similar deletion constructs from the 16 amino acids of the E-T 1 of a dengue virus as disclosed by [Mukhopadhyay]." Final Act. 10.

Appellants contend that Hernandez fails to teach or suggest deletion mutations in the flaviviral E-T1 domain and does not suggest that the deletions are made relative to a central glycine region. Appeal Br. 11; Reply Br. 3. Appellants argue that Hernandez teaches away from making deletions in the E-T domain. Appeal Br. 12–15.

Legal Principles

> In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. "[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." The patent applicant may then attack the Examiner's *prima facie* determination as improperly made out, or the applicant may

> present objective evidence tending to support a conclusion of nonobviousness.

In re Fritch, 972 F.2d 1260, 1265 (Fed. Cir. 1992) (alteration in original) (citations omitted).

Analysis

We agree with Appellants that the Examiner has failed to establish a prima facie case of obviousness. The Examiner has not pointed to, nor have we discerned, any teaching in the references that would lead one skilled in the art make the specific deletions recited in the claims about central glycine moiety.

While we agree with the Examiner that Hernandez teaches the general concept of making deletions in envelope proteins in viruses such as flaviviruses, as Appellants point out, there is no teaching or suggestion to make the deletions in the E-T1 domain. Appeal Br. 6–7. Moreover, there is nothing in Hernandez that would suggest making the deletions about a central glycine moiety. Figure 4 of Hernandez cited by the Examiner teaches deletions about a central methionine moiety not a glycine moiety. Hernandez, FIG. 4. The Examiner has offered no evidence to show why one skilled in the art would select glycine as the central amino acid.

The Examiner cites to Mukhopadhyay as teaching a central position of the E-T1 domain. Ans. 7. We are not persuaded. While Mukhopadhyay might teach the numbers of the amino acids in the E-T1 transmembrane domain, nowhere does Mukhopadhyay teach the specific identity of the amino acids in the domain. Mukhopadhyay 13. There is nothing in

Mukhopadhyay that would lead on skilled in the art to use a glycine moiety as the center point for the recited deletions.

Conclusion

We conclude that a preponderance of the evidence does not support the Examiner's finding that claims 1–10 would have been obvious over Hernandez combined with Mukhopadhyay and Pugachev.

SUMMARY

We reverse the rejection under 35 U.S.C. § 101.

We reverse the rejection under 35 U.S.C. § 103(a).

REVERSED