

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PISANO CLAUDIO

Appeal 2008-5486
Application 10/949,194
Technology Center 1600

Decided: December 22, 2008

Before ERIC GRIMES, RICHARD M. LEBOVITZ, and STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of using carnitine to increase transfected gene expression. The Examiner rejected the claims for failure to enable using the invention as broadly as it is claimed. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

The invention relates to using acetyl L-carnitine (ALC) in the production of recombinant proteins. (Spec. 1.) Treating cells with ALC is

said to increase the expression of proteins coded for by liposome mediated transiently transfected genes. *Id.*

Claims 1 and 9 are on appeal.¹ Claim 1 is representative and reads as follows:

1. A method for increasing expression of liposome mediated transiently transfected genes in cells comprising the administration of acetyl L-carnitine.

The Examiner rejected the claims under the enablement requirement of 35 U.S.C. § 112, first paragraph.

ENABLEMENT

The Enablement Issue

The Examiner rejected claims 1 and 9 under 35 U.S.C. § 112, first paragraph, on the ground that the Specification does not enable a person skilled in the art to use the invention as broadly as it is claimed. The Examiner's position is that although the invention can be used *in vitro*, undue experimentation would have been required to use the invention *in vivo*. (Ans. 4-8.)

Appellant contends that liposome mediated transient transfection of genes into cells is a well known technique, applicable to cells whether they are cultured outside an animal or present in an animal. (App. Br. 4.) According to Appellant, the invention is an improvement on known *in vivo*

¹ Claim 7 is also pending and indicated allowable (App. Br. at 2).

liposome mediated transient transfection protocols, and in vivo oral dosing could be optimized without undue experimentation. (App. Br. 5.)

The issue with respect to this rejection is whether undue experimentation would have been required to practice in vivo embodiments of the method.

Findings of Fact

1. The Specification states that treatment with ALC in cell clones transfected using known techniques such as liposomes increases the protein expression of the transfected genes. (Spec. 1.)
2. An in vitro experiment transfecting HeLa cells in vitro with a luciferase gene was described. (Spec. 2-4.)
3. Results of the HeLa cell experiment showed that ALC caused an increase in luciferase gene expression. (Spec. 5-6.)
4. The Specification indicates that results of slot blot densitometry of the HeLa experiment “showed that the presence of ALC did not change the cellular uptake of the DNA/Liposome complex suggesting that the ALC could affect the expression of luciferase at transcriptional level.” (Spec. 10.)
5. The Specification describes in vivo experiments in which mice were treated with ALC for four days prior to transfection. (Spec. 4.)
6. After transfection, lung tissue was collected from the mice. (Spec. 4.)

7. The Specification does not report protein expression results from the in vivo experiment with mice.
8. The Examiner relied on the Eastman² and Wang³ references as evidencing the state of the art. (Ans. 6.)

Principles of Law

The first paragraph of 35 U.S.C. § 112 requires a patent specification to contain a description of the manner of using the invention “in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains” to use the invention. The statute requires that the specification teach persons skilled in the art to use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The disclosure must provide sufficient guidance to enable those of skill in the art to use the invention as broadly as claimed. *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991). Assuming there is sufficient reason to think undue experimentation would be needed to use an invention, a rejection for failure to teach how to use would be proper. *In re Marzocchi*, 169 USPQ 367, 369-70 (CCPA 1971). “Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. . . . Of course, if the

² U.S. Patent No. 6,465,007 B1, issued Oct. 15, 2002.

³ Jinkang Wang et al., *Synthesis and Characterization of Long Chain Alkyl Acyl Carnitine Esters. Potentially Biodegradable Cationic Lipids for Use in Gene Delivery*, 41 J. MED. CHEM. 2207-15 (1998).

number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid.” *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). An inventor’s theory or belief as to how the invention works is not a necessary element in the Specification to satisfy the enablement requirement of 35 U.S.C. § 112. *Cross v. Iizuka*, 753 F.2d 1040, 1042 n.3 (Fed. Cir. 1985).

Analysis

The Examiner accepted that in vitro embodiments of the claimed method could be used without undue experimentation, but doubted that in vivo embodiments could be made to work without undue experimentation. (Ans. 3.) The Examiner considered it “unclear how the administration of [ALC] in the absence of DNA (i.e. prior or post transfection) could result in increased gene expression and protein production.” (Ans. 7, emphasis added.) The Examiner found that ALC’s “potential to increase *in vivo* expression of a transgene by administering [ALC] pre or post transfection, or in the absence of complexation with lipid would be unpredictable.” *Id.*

The evidence in the Specification is that treating cells with ALC prior to, during, and after transfection led to increased expression of the transfected luciferase gene. (Spec. 2-3.) In the in vitro experiment, the ALC was administered by itself, i.e., not complexed with lipid. *Id.* The result

was increased gene expression. Given that evidence, we are not persuaded of unpredictability when ALC is administered in the absence of complexation with lipid. There is no requirement that an Applicant explain the scientific principles underlying how an invention works. That the Specification teaches how to use the invention is sufficient. *Cross*, 753 F.2d at 1042 n.3.

The Examiner interpreted Eastman and Wang as showing that carnitine derivatives assist transfection only when complexed with lipids or liposomes. (Ans. 7.) Thus interpreted, the prior art might cast doubt on effective use of pre- or post-transfection administration. Eastman does not support that reading. Eastman teaches that cells to be transfected may be treated with tight junction disrupting compounds (such as palmitoyl-carnitine or decanoylcarnitine) “either prior to, simultaneously with, or as part of a pharmaceutical composition.” (Eastman, col. 11, ll. 30-32.) On the other hand, we agree that Wang transfets with liposomes containing long-chain alkyl acyl carnitine esters. (Wang, paragraph bridging 2210-11.) Wang’s results using long-chain carnitine containing liposomes to transfet do not suggest the claimed method would not work for the claimed acetyl L-carnitine. We are not directed to evidence that Wang addressed transfection with carnitine derivatives alone or prior to or following DNA transfection. The claim here is a method for increasing expression of transfected genes, not a method for increasing transfection as Wang described.

Significantly, Appellants explain that their data shows that ALC did not change the cellular uptake of DNA. (FF4.) That ALC does not appear to change DNA uptake weighs against reading Eastman and Wang, both concerning DNA delivery or uptake, as supporting a conclusion of non-enablement for Appellants' method which may not involve DNA uptake. Applicants are usually not required to explain how an invention works, but we note their observation that the ALC might be working at the transcriptional level. *Id.* This evidence-based observation is an additional reason for not inferring that Eastman or Wang weigh against enablement for the claimed method.

The Specification describes an *in vivo* example in which mice were pretreated with ALC and then transfected, although the results of that example are not reported. (FF5-7.) Pretreatment would be consistent with the *in vitro* working example, and with Eastman's teaching. In view of the Specification's evidence, and Eastman's teachings, we are not persuaded that the Examiner's theory about ALC's potential to induce DNA compaction during liposome complex formation (Ans. 7) should receive controlling weight. In view of the disclosure that ALC did not change cellular uptake (FF4), and the guidance provided in the Specification, we are not persuaded that undue experimentation would be needed to use post-transfection embodiments of the invention.

In any event, a claim that encompasses inoperative embodiments is not necessarily nonenabled. In such a case, the question is whether the

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inoperative embodiments would force the skilled artisan to experiment unduly in order to practice the claimed method. In this case, the Examiner has not shown that any inoperative embodiments encompassed by the claims would have forced the skilled artisan to carry out undue experimentation.

CONCLUSIONS OF LAW

We conclude the Office has not established a *prima facie* case that undue experimentation would have been required to practice *in vivo* embodiments of the method.

ORDER

The rejection of claims 1 and 9 under 35 U.S.C. § 112, first paragraph, for lack of enablement is

REVERSED.

Ssc:

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