

The opinion in support of the decision being entered today was not written for publication in a law journal and is not binding precedent of the Board.

Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JAN E. DE VRIES, CHUNG-HER JENH, SATWANT K. NARULA,
and PAUL J. ZAVODNY

Appeal No. 1996-3797
Application No. 08/070,162

ON BRIEF

Before WINTERS, ROBINSON, and ADAMS, Administrative Patent Judges.
ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 - 9, which are all of the claims pending in the case.

Claim 1 is illustrative of the subject matter on appeal and reads as follows:

1. A human cell line cloned from a cell which has been stably transformed by a recombinant vector comprising a reporter gene operatively linked to a human IL-4-responsive element, which responsive element is capable of inducing expression of the reporter gene in response to IL-4.

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The references relied upon by the examiner are:

Hall et al. (Hall), "Expression and Regulation of Escherichia coli lacZ Ghene Fusions in Mammalian Cells," The Journal of Molecular and Applied Genetics, Vol. 2, pp 101-109 (1983).

Mills et al. (Mills), "Sequences of Human Immunoglobulin Switch Regions: Implications for Recombination and Transcription," Nucleic Acids Research, Vol. 18, pp 7305-7316, (1990).

Sambrook et al. (Sambrook), Molecular Cloning - A Laboratory Manual, Cold Spring Harbor Laboratory Press, 2nd Edition, Chapter 16, pp 16.41-16.46 and 16.57-16.58 (1989)

Suter et al. (Suter), "Expression of Human Lymphocyte Ige Receptor (Fc_ERII/CD23)," The Journal of Immunology, Vol. 143, pp 3087-3092 (1989).

Rothman et al. (Rothman), "Identification of a Conserved Lipopolysaccharide-Plus Interleukin -4- Responsive Element Located at the Promoter of Germ Line 0 Transcripts," Molecular and Cellular Biology, Vol. 11, pp 5551-5561 (1991).

Takai et al. (Takai), "DNA Transfection of Mouse Lymphoid Cells by the Combination of DEAE-dextran-mediated DNA uptake and osmotic shock procedure," Biochimica et Biophysicas Acta. Vol. 1048, pp 105-109 (1990).

Grounds of Rejection

Claims 1-5 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Suter, Sambrook, and Takai.

Claims 6-9 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Suter, Sambrook, Takai and Hall.

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Claims 6 and 8 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Suter, Sambrook, Takai, and Rothman.

Claims 1-3, 5, 6, and 8 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Suter, Mills, and Rothman.

Claims 6 and 8 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Suter, Mills, Rothman, Sambrook and Hall.

We reverse.

Background

The applicants describe the presently claimed invention at pages 5-6 of the specification as relating to human cell lines cloned from a cell which have been stably transformed by a recombinant vector comprising a reporter gene operatively linked to a promoter comprising a human IL-4-responsive element. The stable transformed cell line is stated to be useful in detecting human IL-4 agonists and antagonists. Applicants explain that contacting the cell line with a sample containing an IL-4 agonist or an antagonist in the presence of IL-4 results in expression or reduced expression of the reporter gene.

Discussion

The rejections under 35 U.S.C. § 103

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's answer (Paper No.

19) for the examiner's reasoning in support of the rejections and to the appellants' brief (Paper No. 18) and reply brief (Paper No. 20) for the appellants' arguments thereagainst.

Obviousness is a legal conclusion based on the underlying facts. Graham v. John Deere Co., 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966); Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1270, 20 USPQ2d 1746, 1750 (Fed. Cir. 1991); Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1566-68, 1 USPQ2d 1593, 1595-97 (Fed. Cir. 1987). Here, the dispositive question is whether one of ordinary skill in this art at the time of the invention would have found it obvious to prepare a human cell line cloned from a cell which has been stably transformed by a recombinant vector comprising a reporter gene which is operatively linked to a human IL-4 response element that is capable of inducing expression of the reporter gene in response to IL-4.

Critical to all of the examiner's rejections is the disclosure of Suter which the examiner would combine with the remaining references as a basis of establishing a prima facie case of obviousness within the meaning of 35 U.S.C. § 103. The examiner has cited Suter as disclosing the Fc_ERII nucleotide sequence as well as the Fc_ERII IL-4 responsive element and the insertion of this DNA segment into the expression vector pCMVcat, wherein CMV is a promotor and cat is a reporter gene. The examiner urges that Suter describes the transfection of Human Jijoye cells (Compare appealed claim 5) with this plasmid using DEAE dextran method of transfection. (Answer, page 3). The examiner urges that these transformed cells are used to demonstrate that IL-4 induces the expression of FcERII via the assessment of Cat activity. (Answer, page 4). The examiner

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acknowledges that Suter does not teach "the making of a stably transformed cell expressing this vector and making a cell line therefrom." (Id.)

The examiner cites both Sambrook and Takai as teaching the use of the DEAE-dextran method for stable transformation of cells. (Answer, paragraph bridging pages 4-5).

The examiner concludes that (Answer, page 5):

[o]ne of ordinary skill in the art would have been motivated to make the Jijoye cells according to Suter et al. and maintain these cells to determine and acquire stable transformants of the cells for the study of IL-4 and IgE regulation and use as a pharmaceutical screening assay for agents useful in the treatment of allergies because both Sambrook et al. and Takai et al. teach that DEAE-dextran method of transfection can result in stably transformed cells.

Appellants, in rebuttal, argue that (Brief, page 11):

[t]here is no suggestion or even an inference in Suter, et al. that stable transformants should be prepared. Furthermore, there is nothing to suggest that studies alluded to cannot be carried out using transiently transfected cells as described by Suter, et al. Similarly, there is nothing in the secondary references, Sambrook, et al., and Takai, et al., to suggest or motivate the ordinary skilled artisan to combine and modify [these] references.

On balance, we agree with appellants that the rejection, based on the combination of Suter with Sambrook and Takai, is not sustainable. While we do not doubt that the methodology of Sambrook and Takai could have been used in combination with the techniques described by Suter to arrive at a stably transformed cell which could have been

cloned, more is required. The fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, we find no reason stemming from the prior art which would have led a person having ordinary skill to the claimed invention. The examiner proposes that one would be motivated to modify the techniques and cells of Suter to arrive at stably transformed cells in order to more easily maintain a readily available and reliable screening assay system. However, as pointed out by appellants, the examiner offers no evidence and points to no facts to be found in the prior art which would reasonably suggest the need for such a system. In our judgment, the only reason or suggestion to combine the teachings of these references, in the manner proposed by the examiner, comes from appellants' specification. Neither Hall nor Rothman provide that which is missing from Suter, Sambrook, and Takai.

In the remaining rejections under 35 U.S.C. § 103, the examiner has relied upon Suter in combination with Mills and Rothman or Suter in combination with Mills Rothman, Sambrook, and Hall. Mills, Rothman, Sambrook, and Hall do not provide that which we have determined to be missing from the combination of Suter with Sambrook and Takai. To establish a prima facie case of obviousness, there must be more than the demonstrated existence of all of the components of the claimed subject matter. There

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must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge cannot come from the applicants' disclosure of the invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). On the record before us, we find no reasonable suggestion for combining the teachings of the references relied upon by the examiner with Suter in a manner which would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On these circumstances, we are constrained to reach the conclusion that the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness as to the claimed cell line. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore, the rejections of claims 1-9 under 35 U.S.C. § 103 are reversed.

Other issues

In considering the issues raised by this appeal, it is unclear to us whether the examiner has fully appreciated the significance of the disclosure provided by Rothman as it relates, at least, to claim 1. As we read Rothman, this reference describes efforts (page 5553, paragraph bridging columns 1 and 2):

[t]o determine whether sequences that include the normal Ig promoter are sufficient for LPS/IL-4 inducibility, a 1.1 kb genomic *Pst*I fragment, . . . was cloned 5' to the CAT reporter gene in a plasmid with not other eukaryotic promoter (Fig. 2). This construct was stably transfected into the 18.81A20 A-MuLV-transformed pre-B-cell line. Transfectants contained CAT activity only slightly higher than that of untransfected controls, and culture with IL-4 alone or LPS alone did not affect this level of CAT expression (Fig.2, lanes 1, 2, and 4). In contrast, culture of the transfectants in the simultaneous presence of LPS and IL-4 led to a progressive and substantial increase in CAT . . . activity following LPS/IL-4 treatment (Emphasis added)

While this portion of Rothman reasonably describes the stable transformation of a cell with a reporter gene operatively linked to an IL-4 responsive element, the description indicates that the expression of the reporter gene is induced only by the presence of both LPS and IL-4. (Rothman, page 5553, column 2, first full sentence). It does not appear from the record before us that the examiner has determined whether claim 1 can reasonably be read to include inducement of expression of the reporter gene, in a transformed cell, by more than just IL-4 or should be read to be limited to only IL-4 and thus exclude the

presence of additional agents such as LPS of Rothman. In this regard we note pages 13 and 14 of the specification which states:

"For use in Jijoye cells it is preferred that the Fc_ERII IL-4-responsive element be associated with another promoter and/or enhancer element to form a hybrid promoter. . . . The use of a hybrid promoter is desirable when it increases the signal strength of the reporter gene used, while maintaining inducibility by human IL-4.

While we could offer our own interpretation of the claim and reach a conclusion as to the obviousness or anticipation of the claim by this reference, we elect not to do so. We serve as a board of review¹ and leave to the examiner and appellants to interpret the claims of an application in the first instance. However, upon return of the application to the group, we would urge the examiner and appellants to at least consider whether claim 1 as properly interpreted, would be subject to rejection over Rothman, either alone or in combination with other prior art. Should the examiner determine that the claims are unpatentable, the examiner should issue an appropriate communication explaining in detail the basis of such a rejection and provide appellants with an opportunity to respond.

Summary

To summarize, the examiner's rejections of claims 1-9 under 35 U.S.C. § 103 are reversed.

¹ 35 U.S.C. § 7(b)("[t]he [board] shall . . . review adverse decisions of examiners upon applications for patents . . .").

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REVERSED

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Administrative Patent Judge)	
)	
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)	BOARD OF PATENT
Douglas W. Robinson)	
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