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The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte CARY A. WEINBERGER

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Appeal No. 95-2319  
Application 07/812,880<sup>1</sup>

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ON BRIEF

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Before WILLIAM F. SMITH, ELLIS and ROBINSON, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 - 13 and 15 - 21, which are all of the claims pending in this application.

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<sup>1</sup>Application for patent filed December 20, 1991. According to appellant, the application is a continuation of Application 07/426,894, filed October 25, 1989, now abandoned.



Logan et al. (Logan), "Adenovirus tripartite leader sequence enhances translation of mRNAs late after infection", Proc. Natl. Acad. Sci. USA, vol. 81, pages 3655-3659 (June 1984).

### **Grounds of Rejection**

Claims 1-3, 9, 15, 16, and 21 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Evans and Stryer.

Claim 4 stands rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Evans, Stryer and Shackelford.

Claim 5 stands rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Evans, Stryer, and Piccini.

Claims 5-8 and 17-21 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Evans, Stryer, and Jones.

Claims 10-13 stands rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Evans, Stryer, and Logan.

We reverse.

### **BACKGROUND**

At page 4 of the specification, the applicant describes the invention as relating to improvements in a bioassay for identifying and measuring materials having ligand activity toward hormone or hormone-like receptor polypeptides, wherein virally infected host cells are cultured in the presence of a test compound or compounds. The virus is said to comprise DNA encoding a reporter molecule operatively linked to the appropriate, corresponding hormone response element DNA. Where the host cells lack endogenous

quantities of the receptor, the virus further comprise DNA which encode the functional hormone or hormone-like receptor. Applicant explains that the host cells remain viable and produce measurable amounts of reporter molecule, upon induction of the hormone response element by successful ligand complex formation, when a successful ligand material is tested.

**Discussion:**

**Claims:**

Claim 1 is directed to a bioassay for identifying compounds which function as ligands for functional receptor proteins comprising culturing mammalian cells, which have been infected with recombinant virus, in a medium containing the test compound or compounds. The recombinant virus comprise DNA which encode an operative hormone response element operatively linked to DNA encoding reporter. The cultured cells are monitored for expression of the reporter, which is indicative of the ability of the compound being tested to act as a ligand for the receptor peptide. Claim 2 is directed to a bioassay wherein the mammalian host cells are co-infected with recombinant virus comprising DNA encoding the functional receptor and DNA encoding a hormone response element operatively linked to a DNA encoding reporter.

**The rejections under 35 U.S.C. § 103**

**Claims 1-3, 9, 15, 16, and 21:**

Claims 1-3, 9, 15, 16, and 21 stand rejected under 35 U.S.C. § 103 as obvious over Evans in view of Stryer.

In describing Evans, the examiner states (Answer, page 6):

Evans et al teach a method for identifying functional ligands for receptor proteins by transfecting host cells with a chimeric gene which includes operative portions of a DNA-binding domain regions from a ligand-responsive receptor protein and with a reporter gene functionally linked to an operative hormone response element.

The examiner acknowledges that Evans differs from the claimed invention stating (Answer, page 6):

This reference does not teach infection with recombinant virus in order to introduce the genes of interest into the host cell.

The examiner relies on Stryer as teaching that infection with recombinant virus is one of several methods of gene transfer (Answer, page 6). The examiner concludes (Answer, page 6):

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used infection to introduce the genes taught by Evans et al for the assay for functional ligands into the host cells using infection as taught by Stryer.

It is the initial burden of the patent examiner to establish that claims presented in an application for patent are unpatentable. In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). We have carefully considered the evidence and discussion in support of the rejection presented by the examiner. However, a fair evaluation of the references, applicant's specification and consideration of the claimed subject matter as a whole, dictates a conclusion that the construction of the claimed method from the prior art teachings is not suggested by the record before us.

Evans discloses, at columns 11-12, a bioassay for identifying functional ligands for

receptor proteins, wherein a host cell is transfected with a chimeric receptor gene and a reporter gene which is functionally linked to an operative hormone response element. The transfected host cells are challenged with a candidate ligand and induction of the reporter gene is monitored as an indicator as to whether the test compound binds to the receptor protein. Evans does not disclose the use of virally infected cells in the disclosed assay.

As conceded by appellant (Reply Brief, page 6):

. . . the Stryer reference teaches methods for infecting cells with a virus to produce virus-infected cells.

However, we find ourselves in agreement with appellant's statement (Reply brief, page 6):

. . . Stryer indisputably does not suggest using virus-infected cells in a bioassay . . . .

We also agree with appellant that more is needed to support the combination of Evans and Stryer. To establish a prima facie case of obviousness, there 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 can not come from the applicant's 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). The extent to which such suggestion must be explicit in or may be fairly inferred from the references, is decided on

the facts of each case, in light of the prior art and its relationship to the invention. In re

Gorman, 933 F.2d 983, 986-987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

Here, the examiner has provided no evidence or facts which would suggest the use of virally infected cells as taught by Stryer in the bioassay of Evans. We note the examiner's statement at pages 6-7 of the Answer in support of the combination of the teaches of the two references:

. . . because infection and transfection are considered equivalents in gene transfer and because such an infection method was well established in the art so as to be routine enough to give a reasonable expectation of success.

We find this statement less than clear as to whether the examiner's position is that infection and transfection would have been equivalent if used in a bioassay as herein claimed or merely equivalent in gene transfer. Also, it is not clear from the record whether the "reasonable expectation of success" refers to the ability of the two techniques to accomplish gene transfer, or more relevant to the claims on appeal, suggest that one of ordinary skill in this art would have a reasonable expectation of success in obtaining a mammalian cell infected with a virus comprising DNA encoding a hormone response element operatively linked to a DNA encoding reporter alone or with DNA encoding the functional receptor protein which would be useful in the bioassay claimed. The examiner has failed to provide any factual support or evidence which would have reasonably suggested, to one of ordinary skill in this art, the use of the virally infected cells of Stryer in the bioassay process disclosed by Evans other than the disclosure provided by the appellant. Where, as here, 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 rejection of claims 1-3, 9, 15, 16, and 21 under 35 U.S.C. § 103 over Evans and Stryer is reversed.

**Claims 4-8, 10-13 and 17-21:**

Claim 4 stands rejected under 35 U.S.C. § 103 as unpatentable over Evans, in view of Stryer in further view of Shackelford.

Claim 5 stands rejected under 35 U.S.C. § 103 as unpatentable over Evans in view of Stryer in further view of Piccini.

Claims 5-8 and 17-21 stand rejected under 35 U.S.C. § 103 as unpatentable over Evans in view of Stryer in further view of Jones.

Claims 10-13 stand rejected under 35 U.S.C. § 103 as unpatentable over Evans in view of Stryer in further view of Logan.

In rejecting claims 4-8, 10-13, and 17-21 under 35 U.S.C. § 103, the examiner relies on Evans and Stryer, taken in further combination with the individual references noted. In view of our determination regarding the rejection of claims 1-3, 9, 15, 16, and 21 over Evans and Stryer, it is necessary to determine only whether the additional references, relied upon by the examiner, provide that which is missing from Evans and Stryer. They do not. The references do not provide the reason, suggestion, or motivation determined to be missing and necessary to support the combination of the disclosures of Evans and Stryer in a manner which would have lead one of ordinary skill in this art to use the recombinant virus infected cells of Stryer in the bioassay disclosed by Evans. Therefore, with regard to claims

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4-8, 10-13 and 17-21, it is our conclusion that the examiner has failed to established a prima facie case of unpatentability of the claimed subject matter.

The rejections of claims 4-8, 10-13 and 17-21, under 35 U.S.C. § 103, are reversed.

**Summary**

The decision of the examiner to reject claims 1-13 and 15-21 under 35 U.S.C. § 103 is reversed.

**REVERSED**

WILLIAM F. SMITH	)	
Administrative Patent Judge	)	
	)	
	)	BOARD OF PATENT
	)	APPEALS AND
	)	INTERFERENCES
DOUGLAS W. ROBINSON	)	
Administrative Patent Judge	)	
	)	

Ellis, Administrative Patent Judge, concurring-in-part, dissenting-in-part

In the case before us, I agree with the examiner that, given the combined teachings of Stryer and Evans, it would have been prima facie obvious to one of ordinary skill in the art to introduce the claimed DNA molecule into a mammalian cell by infection with a recombinant virus comprising said DNA molecule. The examiner finds, and the appellants do not contest, that Evans teaches the claimed bioassay, but he employs a different method of introducing the DNA into the mammalian cells. That is, Evans transfects the mammalian cells with the DNA molecule using a plasmid vector, rather than infecting with a viral vector. Stryer specifically discloses that the methods of transfection and infection, as a means of introducing a DNA molecule into a mammalian cell, are interchangeable. Thus, absent an unexpected result, I would hold that it would have been obvious to persons of ordinary skill in the art of molecular biology to employ another convenient, conventional method of introducing a DNA molecule into a mammalian cell, such as infection, in the bioassay described by Evans. Accordingly, in my view, the rejection of claims 1, 3, 9 and 15 should be affirmed.

I note the appellants' statement of p. 2 of the Reply Brief, that claims 2, 16 and 21, do not stand or fall with claims 1, 3, 9 and 15. Therefore, for purposes of this appeal, I would consider this aspect of the rejection as it applies to the broadest claim, claim 2. To that end, the appellants argue that the claim requires that the mammalian cells be "co-infected with recombinant virus." Reply Brief, p. 8. However, the claim merely "reads on" the infection of a mammalian cell with two or more of the viruses described in claim 1. Accordingly, I would

also affirm the rejection of these claims over the teachings of Evans and Stryer.

The appellants argue that a major advantage to using the claimed method is that the recombinant virus has the “ability” or “capacity” to infect 100% of the target cells. Brief, pp. 7-8; Reply Brief, pp. 4-5. However, this argument does not address a limitation present in the claims. Moreover, the appellants have not established that this “advantage” actually occurs using the claimed method and that it would not have been expected by those of ordinary skill in this art. For a showing of unexpected results to be probative evidence of nonobviousness, the appellant must establish (i) that there is a difference between the results obtained for the claimed method, and (ii) that the difference obtained is significant and would not have been expected by a person having ordinary skill in the art at the time the invention was made. In re Freeman, 474 F.2d 1318, 1324, 177 USPQ 139, 143 (CCPA 1973); In re D’Ancicco, 439 F.2d 1244, 1248, 169 USPQ 303, 306 (CCPA 1971).

I also agree with the examiner that in view of the teachings of Shackleford and Piccini as to the use of mouse mammary tumor virus (MMTV) and vaccinia, respectively, to infect mammalian cells and to express a heterologous gene therein, it would have been further obvious to employ MMTV or vaccinia as the recombinant vector in the bioassay disclosed by Evans. Accordingly, I would affirm the rejection of claims 4 and 5.

However, with respect to the rejections of claims 5-8 and 17-21 in view of Evans, Stryer and Jones; and claims 10-13 in view of Evans, Stryer and Logan, I part company with the examiner. I do not find that Jones and Logan teach or suggest the claimed limitations. Thus, I find that the examiner has not met her burden of establishing a prima facie case of

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obviousness. Accordingly, I concur with the majority's conclusion that the rejection of these claims should be reversed.

JOAN ELLIS  
Administrative Patent Judge

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