

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 34

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte NANCY H. COLBURN, ZIGANG DONG, POWEL H. BROWN
and MICHAEL J. BIRRER

Appeal No. 2002-1631
Application No. 08/213,433¹

HEARD: January 7, 2003

Before WILLIAM F. SMITH, SCHEINER and GRIMES, Administrative Patent Judges.

SCHEINER, 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 26 through 37. Claims 1 through 6, 10, 13, 14 and 17 through 22, the only other claims pending in the application, have been withdrawn as directed to non-elected subject matter.

Claim 26 is representative of the subject matter on appeal:

26. A method for treating a mammal having a tumor which has AP-1 transcription activity comprising: administering to the mammal a therapeutically effective amount of a DNA construct which encodes a c-jun deletion mutant inhibitory to tumor promoter-induced AP-1 transcription activity.

Claims 26 - 37 stand rejected under the first paragraph of 35 U.S.C. § 112, as

¹ Application for patent filed March 10, 1994.

based on a non-enabling disclosure.

We reverse the rejection.

BACKGROUND

“Chemical carcinogenesis is a multistep process that includes initiation, promotion and progression . . . with the rate-limiting steps in multistage carcinogenesis occurring during the promotion and progression phases. Numerous studies have shown that tumor promotion is a long term process that is partially reversible and that requires chronic exposure to tumor promoter.” Specification, page 1. “[S]everal genes that may be involved in tumor promotion or progression have been shown to respond to AP-1,” a heterodimeric transcriptional activator formed from the phosphoprotein products of two proto-oncogenes: c-jun and c-fos. Id., pages 1 and 2.

“Recent studies of the c-jun proto-oncogene have revealed that the regions critical for transcriptional activation include the dimerization domain, the DNA-binding domain, and an area within the amino terminal half of the c-jun protein that functions as a transcriptional activation domain.” It has been demonstrated that “regions of c-jun required for transcriptional activation are the same as those required for c-jun/ras-induced transformation . . . suggesting that c-jun might transform cells by altering gene expression through dysregulated DNA transcription;” it has also been demonstrated that “a dominant negative c-jun mutant which specifically blocked AP-1 activity also blocked H-ras plus c-jun induced cellular co-transformation.” Specification, page 3.

“[T]he present invention relates to methods of . . . treating carcinogenesis in mammals via the use of dominant negative deletion mutants of c-jun as therapeutic agents.” Specification, page 8. As explained by the examiner, “[t]he invention lies in the realm of gene therapy;” thus, “to be effective, sufficient nucleic acid [] encoding a c-

jun deletion mutant would need to be administered to [a] mammal . . . , [t]he nucleic acid would then need to reach [] tumor cells, be translated into the mutant c-jun phosphoprotein in sufficient quantities to complex with other components to form a mutant AP-1 . . . incapable of binding to the AP-1 element in the promoter sequence, or . . . inducing transcription.” Answer, pages 2 and 3.

DISCUSSION

“The first paragraph of 35 U.S.C. § 112 requires, inter alia, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without ‘undue experimentation.’ In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is ‘undue.’” In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (emphasis in original).

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Following a thorough analysis in keeping with that outlined in In re Wands, the examiner rejected the claims under the first paragraph of 35 U.S.C. § 112, concluding that “[t]he claims are not enabled because the specification fails to provide guidance as

to a treatment regime that would lead to the inhibition of tumor promoter-induced AP-1 transcription activity [sufficient] to provide a therapeutic effect to a mammal,” Answer, page 2.

The examiner concedes that working examples 1 through 7 of the specification demonstrate that “AP-1 induced transcription is inhibited when TAM67 DNA² is expressed” in transfected cells, and that “transgenic mice which express TAM67 . . . do not form papillomas and carcinomas when treated topically with . . . tumor promoting compounds.” Answer, page 5. Thus, it does not appear that the examiner questions whether TAM67 DNA, expressed at sufficient levels, can inhibit tumor promotion and /or progression. Nevertheless, in concluding that the present treatment claims are not enabled, the examiner argues that appellants have merely “provided a laundry list of c-jun deletion mutants . . . dosage amount[s] . . . route[s] of delivery . . . and delivery vehicles” (id., pages 7-8) with “no correlation [to] treatment of tumors or cancers where the tumors or cancers did not contain the TAM67 DNA sequence prior to tumor or cancer induction” (id., page 9, emphasis added).³

If we can summarize the basis of the examiner’s conclusion, it is that “gene therapy in general was regarded as unpredictable by the art at the time of filing,” especially “in the realm of expression and delivery of the gene” (Answer, page 4), and the guidance provided by the specification’s descriptions of treatment protocols and

² TAM67 is a DNA construct encoding a particular c-jun deletion mutant.

³ Example 8 of the specification purports to show that the size of “papillomas and squamous carcinomas . . . decreases in mice treated with [] TAM67 nucleic acid sequence or corresponding protein/peptide” (page 33). Nevertheless, there is no evidence that the experiment described in this example was ever actually performed, and the description of the protocol is so sketchy as to be meaningless. Therefore, we are unable to accord it any weight.

prophylactic examples would not have allowed one skilled in the art to “overcome the art recognized unpredictabilities in gene therapy” (id., page 11) to treat pre-existing tumors, without undue experimentation. In particular, we note the examiner’s reliance on Mulligan,⁴ which “caution[s] that ‘a number of key technical issues need to be resolved before gene therapy can be safely and effectively applied in the clinic.’” Id., page 13.

The references relied on by the examiner support her assertion that many aspects of gene therapy, especially gene delivery and expression, were regarded as highly unpredictable at the time the present application was filed, and we accept, for the sake of argument, that the amount of experimentation required to practice the claimed invention would have been considerable. Nevertheless, we believe that in this case, these factors figure too heavily in the examiner’s determination that it would have required undue experimentation to practice the claimed invention. As explained in In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) (citations omitted):

The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. [] The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Similarly, in In re Brana, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995), the court articulated a relativistic (or contextual) standard of enablement based on the nature of the invention and the state of the art:

. . . Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans.

⁴ Mulligan, R.C., “The Basic Science of Gene Therapy,” Science, Vol. 260, pp. 926-932 (May 14, 1993).

Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer. ^[5, 6]

Brana, 51 F3d at 1568, 34 USPQ2d at 1442-43 (citations omitted, footnotes added).

The court also expressed its “firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment of humans” (quoting In re Krimmel, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961)). We recognize that the claims in Brana were directed to chemical compounds taught to be useful in treating cancer, but we believe that the contextual standard discussed in the case is consistent with In re Wands, and is appropriately applied to the present claims directed to methods of gene therapy.

Here, there is evidence of record that numerous gene therapy trials - some involving vectors and protocols similar to those described in the present specification, some involving genes encoding other nuclear proteins - were ongoing or approved at the time of filing, despite the unpredictability of delivery and expression (see Exhibit B, which accompanied appellants’ amendment of September 8, 1997 (paper no. 14)). We regard these trials, ongoing or approved at the time of the invention, as evidence that

⁵ Phase I testing involves administration of a drug to a limited number of humans in order to evaluate its safety. In Phase II testing, the drug is administered to a larger population and its safety and potential efficacy under different dosage regimes are determined.

⁶ Although the court in In re Brana discussed the issues raised in the appeal in the context of utility under 35 U.S.C. § 101 and enablement under the first paragraph of 35 U.S.C. § 112, the rejection before the court was for lack of enablement.

the sort of experimentation required to practice the claimed invention would have been viewed as reasonable by those skilled in the art, and also as evidence that the field had reached that stage of “[u]sefulness in patent law” described in In re Brana, despite a general recognition of the unpredictability of gene therapy.

In our view, the examiner has not established that the experimentation required to practice the claimed invention would have been undue, and therefore impermissible, in this art, where a considerable amount of experimentation would have been regarded as acceptable. Accordingly, the rejection of claims 26 through 37 under the first paragraph of 35 U.S.C. § 112 is reversed.

REVERSED

)	
William F. Smith)	
Administrative Patent Judge)	
)	
)	BOARD OF PATENT
)	
Toni R. Scheiner)	APPEALS AND
Administrative Patent Judge)	
)	INTERFERENCES
)	
)	
Eric Grimes)	
Administrative Patent Judge)	

William S. Feller
Morgan & Finnegan
345 Park Avenue
New York, NY 10154

