

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JACK A. ROTH, TAPAS MUKOPADHYAY,
and MICHAEL TAINSKY

Appeal No. 1996-2756
Application No. 07/987,235

ON BRIEF¹

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

ADAMS, 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 12, 13, 16, 25 and 30-32, which are all the claims pending in the application.

¹ We note appellants waived (Paper No. 32, received March 20, 2001) their request for oral hearing (Paper No. 28, received July 7, 1995). Accordingly, we considered this appeal on Brief.

Claims 12 and 25 are illustrative of the subject matter on appeal and are reproduced below:

12. An antisense RNA molecule which selectively inhibits the expression of the p21 K-ras oncogene, the antisense RNA molecule comprising sequences complementary to exons II and III and intron II of the p21 K-ras oncogene.
25. A nucleic acid molecule which selectively inhibits the expression of the p21 K-ras oncogene, the nucleic acid molecule encoding an antisense RNA molecule comprising sequences complementary to exons II and III and intron II of the p21 K-ras oncogene, the antisense coding region of the nucleic acid molecule being positioned under the control of the β -actin promoter.

The references relied upon by the examiner are:

Weinberg et al. (Weinberg) 4,740,463 Apr. 26, 1988

Izant et al. (Izant), "Inhibition of Thymidine Kinase Gene Expression by Anti-Sense RNA: A Molecular Approach to Genetic Analysis," Cell, Vol. 36, pp. 1007-1015 (1984)

GROUND OF REJECTION

Claims 12, 13, 16, 25 and 30-32 stand rejected under 35 U.S.C. § 103 as being unpatentable over Weinberg in view of Izant.

We reverse.

DISCUSSION

In reaching our decision in this appeal, we considered appellants' specification and claims, in addition to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer² for the examiner's reasoning in support of the rejection. We further reference appellants'

² Paper No. 26, mailed June 6, 1995.

Brief³, and appellants' Reply Brief⁴ for the appellants' arguments in favor of patentability.

Background:

According to the appellants' specification (page 6) the claimed invention provides "a novel approach to the design of antisense RNA molecules, and their coding sequences, in a manner which allows their use to inhibit the expression of specific genes." Appellants' specification (bridging paragraph, pages 6-7) proposes that the claimed invention "will allow that [sic] the development of antisense technology having a much improved ability to inhibit specific gene expression, particularly in those instances where one desires to selectively inhibit a particular gene over that of closely related genes or other members of a gene family." Appellants' specification (page 7) discloses that:

[a] principle [sic] feature of the present invention is the antisense RNA molecules themselves, which include a region that is complementary to and is capable of hybridizing with an intron region of the gene whose expression is to be inhibited. The inclusion of intron-complementary regions in the antisense RNA constructs of the present invention is believed to be the key to both an improved inhibitory capability as well as selectivity.

...

Thus, where intron regions between two genes are distinct, antisense introns can be designed which will hybridize selectively to a selected gene family member, and not to other family members, and thereby inhibit selectivity.

At page 9, the specification further discloses that "[t]he most preferred oncogenes for application of the present invention will be those which exist as a family of genes, where one desires to selectively inhibit one member of a family

³ Paper No. 25, received February 27, 1995.

over other members. In this regard, one may mention by way of example, the ras, .. [family] of oncogenes. ... [T]he ras family, involves the activation of protooncogenes by a point mutation, which apparently results in the expression of a biologically abnormal product.

THE REJECTION UNDER 35 U.S.C. § 103:

We begin our review of the rejection of record in light of the disclosure provided by appellants' specification. According to the examiner (Answer, page 4) Weinberg discloses "an antisense oligonucleotide which selectively inhibits the K-ras oncogene, which encodes a protein of 21,000 molecular weight or p21." The examiner notes (id.) that Weinberg discloses that "[t]ransfection of nucleic acid molecules containing K-ras cDNA in the antisense orientation into SW-2-3 cells ... resulted in the loss of the transformed phenotype normally exhibited by SW-2-3 cells." The examiner further notes (id.) that Weinberg discloses that "the muscle actin promoter would be sufficiently active to produce antisense oncogene transcripts in a quantity sufficient to inhibit the target oncogene." According to the examiner (Answer, page 5) Weinberg "does not teaches [sic] the inhibition of oncogenes by antisense oligonucleotides to introns."

To make up for the deficiency in Weinberg, the examiner applies (Answer, page 5) Izant to teach "that antisense RNA to introns, exons and splice junctions

⁴ Paper No. 27, received July 7, 1995.

will contribute to anti-message inhibition. Therefore, the examiner concludes (id.) that:

given the teachings of the cited prior art the ordinary artisan at the time of the instant invention would have been provided a reasonable expectation of success in making an antisense RNA molecule and a nucleic acid molecule to which selectively inhibits the K-ras oncogene, where the antisense oligonucleotides comprising oligonucleotides to exons II and III, and intron II of the p21 K-ras oncogene.

In response to the examiner's rejection, appellants argue (Brief, page 5) that the cited references fail to suggest the recited intronic and exonic elements of the appealed claims. In addition, appellants argue (id.) that "the prior art indicates that a solution to the problem of target specificity lies in providing specially-engineered, compensatory constructs that are not affected by antisense treatment, not in providing antisense constructs that discriminate between mutant and normal forms of the target gene."

As set forth in Ecolchem Inc. v. Southern California Edison, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075 (CAFC 2000) the:

"[S]uggestion to combine may be found in explicit or implicit teachings within the references themselves, from the ordinary knowledge of those skilled in the art, or from the nature of the problem to be solved." ... However, there still must be evidence that "a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." ... "[A] rejection cannot be predicated on the mere identification ... of individual components of claimed limitations. Rather particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.".... [Citations omitted].

On this record, appellants argue (Brief, page 9) that Weinberg “is completely silent on the use of any particular region of K-ras. This fact, coupled with the silence of the secondary reference on the use of these particular portions of K-ras, render the rejection suspect.” In the regard, we note that the examiner’s statement of the rejection merely concludes (Answer, page 5) that the antisense oligonucleotides comprise oligonucleotides to exons II and III, and intron II of the p21 K-ras oncogene. The examiner, however, provides no support for this conclusion, or explanation as to why one would necessarily include these particular regions.

Furthermore, the claimed invention is directed to a “molecule which selectively inhibits the expression of the p21 K-ras oncogene.” According to the specification (page 7) this molecule “hybridize[s] selectively to a selected gene family member, and not to other family members, and thereby inhibit[s] selectivity.” As appellants argue (Brief, page 9) “rather than designing an antisense construct that specifically targets the ras oncogene, ... Weinberg proposes construction of an artificial proto-oncogene that will escape the indiscriminate effects of a non-specific antisense message.” In response, without directing our attention to a particular portion of the reference, the examiner argues (Answer, page 7) that Weinberg “clearly indicates that it is not always necessary to compensate by the addition of wild type sequences.” The examiner also directs our attention (id.) to Weinberg’s disclosure of “antisense sequences which inhibit expression of the unspliced RNA” and Izant’s teaching

“that anti-sense RNA complementary to introns and splice junctions would contribute to antimessage [sic] inhibition.” However, these arguments fail to address appellants’ argument concerning selective inhibition, specifically the ability to inhibit expression of a specific gene among a family of genes, without affecting the expression of the other gene family members.

With regard to Izant, appellants argue (Brief, bridging paragraph, pages 10-11) that “the sum total of Izant & Weintraub’s contribution to this topic is the comment that ‘indeed, anti-sense RNA complementary to introns, splice junctions, and untranslated mRNA domains may augment our understanding of mRNA processing as well as contribute to anti-message inhibition.’” We remind the examiner that “it is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art.” In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965); see also In re Mercer, 515 F.2d 1161, 1165-66, 185 USPQ 774, 778 (CCPA 1975).

The full paragraph from Izant that contains the sentence relied upon by the examiner reads as follows:

The value of anti-sense transcription as a tool for genetic analysis will become clearer as additional genes and other recipient cell types are examined. While HSV-TK is an informative model system, it is not necessarily the ideal paradigm for most eucaryotic genes particularly because it lacks introns. Indeed, anti-sense RNA complementary to introns, splice junctions, and untranslated mRNA domains may augment our understanding of mRNA processing as well as contribute to anti-message inhibition [citation omitted].

In our opinion, in this context, Izant provides nothing more than an invitation to experiment to develop a better understanding of anti-message inhibition. As set forth in In re O'Farrell, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) "what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." However, "obvious to try" is not the standard for obviousness under 35 U.S.C. § 103.

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 the record before us, we find no suggestion to combine the teachings of the references relied upon by the examiner in a manner which would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. Therefore, in our opinion, the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness. 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).

We further note the declaration of Roth, Mukhopadhyay and Tainsky. In view of this declaration appellants argue (Brief, page 15) that "the declarants reported that an intron-containing antisense construct according to the present invention was significantly more effective at inhibiting tumor cell proliferation than an intronless construct." Appellants further argue (id.) that "the declaration demonstrates that constructs according to the present invention were significantly less toxic to cells

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than the closest prior art.” In response, the examiner argues (Answer, bridging paragraph, pages 9-10) that “[i]t is noted that the declaration is directed to support claims to a composition, not claims to a method. The antisense oligonucleotides used in the declaration would have been obvious to the ordinary artisan at the time of the instant invention for the reasons given above....” In our opinion, the examiner has not adequately addressed appellants’ declaration. We remind the examiner that a conclusion of prima facie obviousness does not end a patentability determination under 35 U.S.C. § 103. As set forth in In re Hedges, 783 F.2d 1038, 1039, 228 USPQ 685, 686 (Fed. Cir. 1986):

If a prima facie case is made in the first instance, and if the applicant comes forward with reasonable rebuttal, whether buttressed by experiment, prior art references, or argument, the entire merits of the matter are to be reweighed. In re Piasecki, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984).

To the extent that the examiner argues that the declaration is not relevant to the composition, we note that “[f]rom the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same.” In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963). In this regard, the examiner should have reevaluated her prima facie case after full consideration of the declaration, along with entirety of the facts and arguments of record. Even had a prima facie case of obviousness had been made in the first instance, in view of the evidence of record, such a prima facie case of obviousness of record would not be sustainable.

Accordingly, we reverse the rejection of claims 12, 13, 16, 25 and 30-32 under 35 U.S.C. § 103 as being unpatentable over Weinberg in view of Izant.

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REVERSED

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Administrative Patent Judge)	
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)	BOARD OF PATENT
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Administrative Patent Judge)	APPEALS AND
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