

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

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(2) is not binding precedent of the Board.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. 40

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GUNTHER SCHUMACHER
MICHAEL JARSCH and WINFRIED BOOS

Appeal No. 1996-1093
Application 07/300,357¹

ON BRIEF

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

ADAMS, Administrative Patent Judge.

¹ Application for patent filed January 23, 1989. The application claims priority to PCT/EP88/00446, filed May 19, 1988 and German Priority document P3716957.2, filed May 20, 1987.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 11, 12, and 44-55, all the claims remaining in the application. Claim 53 is representative of the subject matter on appeal and reads as follows:

53. Isolated nucleic acid molecule consisting of the E. coli or S. Typhimurium mg1 promoter/operator region up to, but not including the ATG codon which is the initiation point of translation of an mg1 operon.

The references relied upon by the examiner are:

Muller et al. (Muller), "Characterization of the Salmonella typhimurium mg1 Operon and its Gene products," Journal of Bacteriology, Vol. 163, pages 37-45 July 1985.

Scripture et al. (Scripture), "The Nucleotide Sequences Defining the Signal Peptides of the Galactose-binding Protein and the Arabinose binding Protein," Journal of Biological Chemistry, Vol. 258, pages 10853-10855 September 1983.

Yanisch-Perron et al. (Perron), "Improved M13 phage cloning vectors and host strains: nucleotide sequences of the M13mp18 and pUC19 vectors," Gene, 1983 pages 103-119.

Waye et al. (Waye), "EcoK selection vectors for shotgun cloning into M13 and deletions mutagenesis," Nucleic Acids Research, Vol. 13, pages 8561-8571 1985.

Maniatis et al. (Maniatis), "Molecular cloning: a laboratory manual," Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, page 422 1982.

In the Examiner's Answer (Paper No. 32, mailed October 3, 1994) the examiner withdrew all grounds of rejection as they appear in the Final Office Action, in view of a new ground of rejection. Claims 11, 12, and 44-55 are rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Muller, Scripture, Perron, Waye and Maniatis. We reverse.

DISCUSSION

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, and the Supplemental Examiner's Answer (Paper No. 37, mailed June 3, 1995) for the examiner's reasoning in support of the rejection. We further reference appellants' Brief (Paper No. 31, filed July 5, 1994), and appellants' Reply Brief (Paper No. 33, filed January 5, 1995) for the appellants' arguments in favor of patentability.

At pages 3-4 of the Examiner's Answer, the examiner states that "Muller teaches an expression vector containing the promoter/operator, initiation region, and signal sequence of the *mgIB* gene from Salmonella typhimurium." At page 4 of the Examiner's Answer, the examiner states that "Scripture teaches the cloning and sequencing of the E.coli mgIB gene and delineates the initiation region and signal sequence." At page 4 of the Examiner's Answer the examiner notes that "[t]he prior art does not explicitly teach the nucleotide sequence encoding the promoter/operator region of the *mgIB* gene from E. coli or S. typhimurium [sic, St.], and its insertion into an M13 vector containing a polylinker . . .

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Delineating the precise nucleotide sequence for the mglB regions utilized by Muller would have been obvious in view of the sequencing of the mglB initiation region and gene (including delineation of the signal sequence) as taught by Scripture.” At page 5 of the Examiner’s Answer, the examiner states, “[i]t would have been obvious to use the mglB gene of Muller or Scripture, with further routine delineation of the promoter/operator region of the Scripture E.coli mglB gene.” The examiner concludes, at page 5 of the Examiner’s Answer, last paragraph, that “[s]ince the vector and polylinker were well known, it would have been obvious to construct the same vector to which the mglB promoter/operator signal sequence and an operably linked gene of interest are added utilizing routine cloning techniques.”

In rejecting claims under 35 U.S.C. § 103, it is incumbent upon the examiner to establish a factual basis to support the legal conclusion of obviousness. *In re Fine*, 837 F.2d 1071, 1073, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Moreover, 35 U.S.C. § 103 requires that the determination of obviousness be made upon a comparison of the “subject matter sought to be patented” and “the prior art.” *See, In re Kratz*, 592 F. 2d 1169, 201 USPQ 71, 76 (CCPA 1979). We find that the examiner did not establish a sufficient factual basis to support the legal conclusion of obviousness.

The claimed invention is directed to an “[i]solated nucleic acid molecule consisting of the E. coli or S. typhimurium mgl promoter/operator region up to, but not including the ATG codon which is the

initiation point of translation of an *mgl* operon,” and expression vectors containing this nucleic acid molecule. Muller provides a partial restriction map of the *S. typhimurium* *mgl* operon, and demonstrates that various *mgl-lacZ* fusion constructs can be expressed. However, the Muller reference does not characterize the *S. typhimurium* *mgl* promoter/operator region, nor does it describe a fusion construct that lacks sequences coding for mature *mglB* protein. At best, Muller teaches, at page 40, “[a]ccordingly, the beginning of the *mgl* operon was located within 0.7 kb between the left *EcoRI* site and the fusion joint of the earliest *mglB-lacZ* fusion (fusion 506).” To overcome this deficiency, the examiner states that “[d]elineating the precise nucleotide sequence for the *mglB* regions utilized by Muller would have been obvious in view of the sequencing of the *mglB* initiation region and gene (including delineation of the signal sequence) as taught by Scripture.” *See*, Examiner’s Answer, page 4.

It appears that the examiner has taken the position that since Scripture sequences a portion of the *E. coli* *mglB* gene region it would have been obvious to sequence Muller’s *S. typhimurium* *mgl* operon, to determine first, the location, and then, the sequence of the promoter/operator region of *S. typhimurium*. Scripture, however, is silent regarding the promoter/operator region of the *E.coli* *mgl* gene region. At page 10854, Scripture states, “[b]etween 5 and 9 nucleotides preceding the initiating ATG codon one finds a characteristic ribosome-binding site (Shine and Dalgarno, 1974). Initiation of transcription would probably occur in the AT-rich region 30

to 40 residues preceding the initiation of translation.” Scripture merely lists the sequence of nucleotides 1-72 (Scripture, Figure 3) which appear to correspond at least in part to the claim language in that this 72 nucleotide sequence is 5’ of the ATG codon of the mglB signal sequence, and the claims are drawn to a “region up to, but not including the ATG codon.” However, lacking in both Muller and Scripture is any reference to a mgl promoter/operator region that would allow a person of ordinary skill in the art to obtain this region as claimed. Therefore, we can not agree with the examiner’s conclusion that “[d]elineating the precise nucleotide sequence for the mglB regions utilized by Muller would have been obvious in view of the sequencing of the mglB initiation region and gene (including delineation of the signal sequence) as taught by Scripture.” *See*, Examiner’s Answer, page 4.

To the extent that the references could be combined as the examiner argues, the combination is inconsistent with the proper standard for obviousness. The mere 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 Laskowski*, 871 F.2d 115, 117, 10 USPQ2d 1397, 1398-99 (Fed. Cir. 1989); *In re Gordon*, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984).

The examiner cites *In re Keller*, 642 F. 2d 413, 425, 208 USPQ 871, 881 (CCPA 1981), at page 2 of the Supplemental Examiner’s Answer, for the proposition that “the test [for obviousness] is what the combined teachings of the references would have suggested to those of ordinary skill in the

art.” In this instance, contrary to the examiner’s position, Scripture and Muller taken together, or individually, would not suggest the claimed mgl promoter/operator region.

To emphasize his position, the examiner states at page 5 of the Examiner’s Answer, “[i]n fact, the mglB gene sequence of E. coli from Scripture (see Figure 3 of Scripture or Figure 12 of the instant application) and the S. typhimurium [sic] mglB gene sequence of the instant application as shown in Figure 1 are identical (both at the nucleotide and amino acid level), and thus they are the same gene and would have been expected to have the same biological activity.” We can not agree with the examiner’s comparison of the two sequences. Upon comparison of Scripture, Figure 3, and Figure 1 of the instant application, it is readily apparent that the sequences *are different* in both their nucleotide and amino acid sequence. Initially, the signal sequence contains two amino acid differences: Amino Acid 15 is Leu in S. typhimurium versus Met in E. coli; and amino acid 20 is His in S. typhimurium versus Ala in E. coli. Similarly, while there are regions of identity between the E. coli and S. typhimurium nucleic acid sequences there are large regions that differ in sequence. For example, compare appellants’ Figure 1, sequence 633-704, with sequence 1-72 of Scripture, Figure 3. Furthermore, Muller, states at page 41, that [i]n comparing our restriction analysis of the S. typhimurium mgl operon with the corresponding analysis of the E. coli operon, no similarities could be observed. The difference in sequence and restriction map between S. typhimurium and E. coli further detracts from the examiner’s position.

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As discussed above the applied prior art fails to teach or suggest the claimed promoter/operator region. Without this region, the claimed plasmids and expression vectors can not be obtained.

Therefore, we find the examiner has not met his burden of establishing a *prima facie* case of obviousness. Having concluded that the examiner has not established a *prima facie* case of obviousness, we do not reach the rebuttal evidence discussed in appellants' Brief (pages 12-14) and Reply Brief (pages 4-6).

OTHER ISSUES

The Communication from the Office mailed March 8, 1993 (Paper No. 21), in response to appellants' petition, filed October 2, 1992 (Paper No. 20), states that the Amendments of April 10 (Paper No. 8), July 6 (Paper No. 13) and August 3, 1992 (Paper No. 16) were entered. Upon review of the application, it does not appear that these Papers were entered as stated in the March 8, 1993 (Paper No. 21) Communication. The examiner should determine the status of these amendments, and take the appropriate action.

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No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

Sherman D. Winters)
Administrative Patent Judge)
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William F. Smith) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
) INTERFERENCES
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Donald E. Adams)
Administrative Patent Judge)

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