

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 30

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ULRICH BRINKMANN, RALF MATTES,
and STEPHAN FISCHER

Appeal No. 1996-0449
Application No. 08/009,423

ON BRIEF

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

DECISION ON APPEAL

This is a decision on appeal from the examiner's final rejection of claims 83-92, which are all of the claims pending in this case. Independent claim 83 is illustrative of the subject matter on appeal and reads as follows:

83. Method for increasing production of a protein which contains arginine, comprising:

(i) transforming an Escherichia coli host cell with an expression vector which contains a DNA sequence, wherein said DNA sequence (a) codes for said arginine containing protein, and (b) contains codons AGG and AGA;

(ii) transforming said Escherichia coli host cell with an extrachromosomal expression vector which contains a DNA sequence which codes for a tRNA, wherein said tRNA (a) incorporates arginine into protein, (b) recognizes both of codons AGA and AGG, and (c) contains anticodon UCU, and

(iii) treating said transformed host cells under conditions favoring an increase in expression of said DNA sequence which codes for said tRNA, so as to produce said arginine containing protein in an amount greater than the amount of said arginine containing protein produced by said host cell prior to transformation.

The references relied upon by the examiner are:

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|------------------------|-----------|---------------|
| George et al. (George) | 4,673,641 | June 16, 1987 |
| Huala et al. (Huala) | 4,970,147 | Nov. 13, 1990 |
| Tabor et al. (Tabor) | 5,145,776 | Sept. 8, 1992 |

Neill et al. (Neill), "Expression of a Wheat " -Gliadin Gene in Saccharomyces cerevisiae," Gene, Vol. 55, pp. 303-17 (1987).

Miller et al. (Miller), "Protein Modification," Journal of Cellular Biochemistry, Supplement 11C, page 195 (1987).

Garcia et al. (Garcia), "The E. coli dnaY Gene Encodes an Arginine Transfer RNA," Cell, Vol. 45, pp. 453-59 (1986).

Robinson et al. (Robinson), "Codon Usage Can Affect Efficiency of Translation of Genes in Escherichia coli," Nucleic Acids Research, Vol. 12 (17), pp. 6663-671 (1984).

Bonekamp et al. (Bonekamp), "The AGG Codon is Translated Slowly in E.coli Even at Very Low Expression Levels," Nucleic Acids Research, Vol. 16 (7), pp. 3013-024(1988).

Appeal No. 1996-0449
Application 08/009,423

Ulrich et al. (Ulrich), "Strains Overproducing tRNA for Histidine," Molecular and General Genetics, Vol. 205, pp. 540-45 (1986).

GROUND OF REJECTION

Claims 83 and 86-90 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Neill, Miller, Garcia, Robinson, Bonekamp and Ulrich.

Claims 84, 85, 91, and 92 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Neill, Miller, Garcia, Robinson, Bonekamp, Ulrich, George, Huala, and Tabor.

We reverse.

BACKGROUND

At pages 3 and 4 of the Specification, applicants describe the invention as relating to a process for expressing a recombinant gene, which contains codons AGA and/or AGG, in Escherichia coli after transformation with an expression vector which contains the recombinant gene wherein the amount of tRNA present in the E.coli host cells is increased by introducing into the cells an additional DNA sequence coding for such tRNA.

DISCUSSION

The rejections under 35 U.S.C. § 103

In considering the issues raised by this appeal, we have considered the Examiner's Answer, the references relied on by the examiner, Appellants' Brief and Reply Brief, as well as the record as a whole. In so doing, we agree with appellants that the rejections of record are based on hindsight reconstruction of the claimed subject matter.

The examiner has cited Neill as teaching a method for increasing production of a protein which contains the amino acid glutamine, wherein a S. cerevisiae host cell is transformed with a expression vector containing a DNA sequence which codes for " -gliadin, the protein containing glutamine. Neill attributes the low production of the recombinant protein to the codon usage pattern of the protein's mRNA and the low concentration of the tRNA required for translation of the " -gliadin mRNA. Neill is said to suggest using tRNA overproducing strains to overcome this limitation. (Answer, page 4). The examiner acknowledges that Neill does not disclose the steps of transforming the host cell with an expression vector containing a DNA sequence which codes for tRNA, wherein the tRNA incorporates arginine into protein, recognizes both codons AGA and AGG, and contains the anticodon UCU, as well as treating the transformed host cells to express said DNA sequence coding for the tRNA in an amount greater than the amount of tRNA present in the host cells prior to transformation. (Answer, paragraph bridging pages 4-5).

The examiner cites Miller, Garcia, Robinson, Bonekamp and Ulrich as evidencing facts directed to the various aspects of the claimed invention and then concludes that (Answer, page 6):

[i]t would have been obvious to modify the disclosure of Neill et al by transforming E. coli as a host cell with a vector containing the tRNA gene which recognizes the AGG or AGA codons (i.e. dnaY), since Miller et al teach the transformation of E. coli with genes encoding tRNA, Robinson et al and Bonekamp et al teach that the AGG codon limits the translation in E. coli of proteins whose corresponding mRNA contain it, and since Garcia teaches the gene encoding the tRNA which inserts arginine at said AGG codon (i.e. dnaY).

What is missing from the examiner's explanation of this rejection is any reason or suggestion to be found in the prior art which would reasonably suggest bringing the unrelated factual evidence together in a manner to arrive at the claimed invention. 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). In order to meet the burden of establishing a prima facie case of unpatentability of the claimed subject matter the examiner must establish that there is a reason, based on the prior art, or knowledge generally available in the art, as to why it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297 n.24, 227 USPQ 657, 667 n.24 (Fed. Cir. 1985). On the record before us, the examiner has failed to provide any evidence which would have reasonably led one of

ordinary skill in this art to modify the method of Neill by substituting E. coli for the disclosed S. cerevisiae, transforming either organism with an additional extrachromosomal expression vector which includes a DNA which codes for a tRNA which recognizes both codons AGA and AGG and contains UCU, and treating the transformed host cells under conditions favoring an increase in expression of the DNA which codes for said tRNA as claimed.

George, Huala and Tabor, additionally relied on in the second rejection under 35 U.S.C. § 103, do not provide that which is missing from the combination of references discussed above.

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 rejections of claims 83-92 under 35 U.S.C. § 103 are reversed. Having determined that the examiner has failed to establish a prima facie case of unpatentability, we have not found it necessary to consider the declaration evidence provided by appellants.

Appeal No. 1996-0449
Application 08/009,423

SUMMARY

The rejections of claims 83-92 under 35 U.S.C. § 103 are reversed.

REVERSED

Sherman D. Winters)
Administrative Patent Judge)
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Teddy S. Gron) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
) INTERFERENCES
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Douglas W. Robinson)
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Appeal No. 1996-0449
Application 08/009,423

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