

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte THOMAS CACECI,
THOMAS E. TOTH
and MARIA B.W. SZUMANSKI

Appeal No. 94-3056
Application 07/812,421¹

HEARD: July 18, 1997

Before WILLIAM F. SMITH, GRON and WEIMAR, Administrative Patent Judges.

WEIMAR, Administrative Patent Judge.

DECISION ON APPEAL

¹ Application for patent filed December 23, 1991. According to applicants, the application is a divisional of Application 07/588,437, filed September 25, 1990, now abandoned.

Appeal No. 94-3056
Application 07/812,421

This is an appeal from the examiner's decision finally rejecting claims 1 and 32-37.

Claim 1 was withdrawn from appeal by Michael E. Whitham, counsel for appellants, at oral hearing before the Board of Patent Appeals and Interferences conducted Friday, July 18, 1997.

Claim 1 being the only claim rejected under 35 U.S.C. § 112, first paragraph, this rejection is moot.

Claims 32-37 remain on appeal and read as follows:

32. A protein having an amino acid sequence defined by blocks 1-6 of Figure 4.

33. A protein having an amino acid sequence defined by blocks 2-7 of Figure 4.

34. A protein having an amino acid sequence defined by blocks 3-8 of Figure 4.

35. A protein having an amino acid sequence defined by blocks 1-8 of Figure 4.

36. A protein as shown in Figure 4.

37. A protein expressed from the plasmid in ATCC deposit No. 68425.

The references relied upon by the examiner are:

Houghten

4,886,663

Dec. 12, 1989

Appeal No. 94-3056
Application 07/812,421

Gourlie et al. (Gourlie), "Winter Flounder Antifreeze Proteins: A Multigene Family," J. Biol. Chem., Vol. 259, No. 23, pages 14960-14965 (1984).

Peters et al. (Peters), "Biosynthesis of Winter Flounder Antifreeze Proprotein in *E. coli*," Protein Eng., Vol. 3, pages 145-151 (1989).

Scott et al. (Scott), "Structural Variations in the Alanine-Rich Antifreeze Proteins of the Pleuronectinae," Eur. J. Biochem., Vol. 168, pages 629-633 (1987).

Gupta et al. (Gupta), "Biological Limitations On the Length of Highly Repetitive DNA Sequences That May Be Stably Maintained Within Plasmid Replicons in *Escherichia coli*," BioTechnology, pages 602-609, September 1983.

Chakrabartty et al., (Chakrabartty), "Structure-Function Relationship In A Winter Flounder Antifreeze Polypeptide," J. Biol. Chem., Vol. 265, pages 11313-11316 (1989).

Williams et al. (Williams), WO 88/05082, July 14, 1988.

Ferrari et al. (Ferrari), WO 88/03533, May 19, 1988.

Shen, "Multiple Joined Genes Prevent Product Degradation in *Escherichia coli*," Proc. Natl. Acad. Sci., Vol. 81, pages 4627-4631 (August 1984).

Doel et al. (Doel), "The Expression in *E. coli* of Synthetic Repeating Polymeric Genes Coding For Poly(L-Aspartyl-L-Phenylalanine)," Nucl. Acids Res., Vol. 8, No. 20, pages 4575-4592 (September 1980).

Kempe et al. (Kempe), "Multiple-Copy Genes: Production and Modification of Monomeric Peptides From Large Multimeric Fusion Proteins," Gene, Vol. 39, pages 239-245 (1985).

Appeal No. 94-3056
Application 07/812,421

Willson et al., "A Simple Method For Constructing Directly Repeated Multimeric DNA Segments," Gene Anal. Techn., Vol. 2, pages 77-82 (1985).

Claims 32-37 stand rejected under 35 U.S.C. § 103 over a combination of all of the above listed references.

We reverse this rejection.

BACKGROUND

Antifreeze polypeptides are known in the art. These polypeptides have been found in fish which live in arctic waters. The polypeptides prevent the formation of ice in their body fluids. See the specification at page 3, lines 8-22. The specification describes a specific protein, shown in Figure 4 of the application, which is a variant of an antifreeze polypeptide found in winter flounder. The prior art describes an antifreeze polypeptide found in winter flounder and its production by bacteria that have been transformed with DNA which encodes the polypeptide. See pages 3 through 6 of the specification.

Claim Interpretation

Before turning to the discussion of the prior art, we set forth our interpretation of claims 32-37.

Claims 32-35 commonly recite: "A protein having an amino acid sequence defined by blocks ... of Figure 4." The only variation in these four claims is that a specific segment of "blocks" from Figure 4 is recited in each one of claims 32-35. The specification refers to the blocks of Figure 4 at page 10, lines 4-16. The blocks are indicated in Figure 4 by two-directional arrows. Blocks 1-8 are contiguous in Figure 4. We hold that each of claims 32-35 represent a genus of proteins of undefined length and unspecified activity, but which must contain the specified amino acids as recited in Figure 4 with the specified "blocks" in contiguous formation as they are shown in Figure 4. While the specification contemplates adding segments which are 11 amino acids in length at the PST1 site shown in block 7 of Figure 4, and such an addition would result in a non-contiguous association of multiple segments (see the specification from page 14, line 15, through page 16, line 1), Figure 4 does not depict these variations, and such variations are not "defined by blocks ... of Figure 4."

Claim 36 recites: "A protein as shown in Figure 4." Page 8 of the specification at lines 22-25, describes Figure 4 as

Appeal No. 94-3056
Application 07/812,421

"a base pair sequence ... and a synthesized amino acid sequence for an AFP polypeptide WF8R wherein the gene wf8r codes for the AFP WF8R" (emphasis added). Page 9 of the specification at lines 20-22, refers to the protein in Figure 4, stating: "Referring now to the drawings, and more particularly to Figure 4, there is shown a synthetic AFP peptide (SEQ ID NO:2)" (emphasis added). Thus, we hold that claim 36 is limited to a single protein which has the amino acid sequence of SEQ ID NO:2.

Claim 37 recites: "A protein expressed from the plasmid in ATCC deposit No. 68425." As stated on page 26, lines 1-4, this deposited plasmid corresponds to "plasmid PgX28L" of the specification. Figure 9 shows the scheme of production of plasmid PgX28L and the scheme is discussed at pages 18-22 of the specification. Claim 37 recites "a protein expressed from the" specified plasmid. We hold that this claim is inclusive of any protein which can be expressed from this plasmid.

DISCUSSION

Claims 32-37 stand rejected under 35 U.S.C. § 103 over Gourlie and Peters in view of Chakrabartty, Houghten and Scott

Appeal No. 94-3056
Application 07/812,421

and further in view of any one of Williams, Ferrari, Shen, Doel, Kempe or Willson.

We reverse this rejection. A prima facie case of obviousness has not been presented by the Examiner.

The combined prior art teachings do not provide a reasonable basis for increasing the number of 11 amino acid sequence repeats in the antifreeze polypeptide of winter flounder to establish that the claimed polypeptides would have been obvious to a person having ordinary skill in the art at the time of the invention. The reasoning presented in the rejection is stated at page 12 of the Examiner's Answer, lines 11-25:

It would have been further obvious to enhance the antifreeze properties of the protein by adding additional repeat sequences as suggested by Chakrabartty or by amino acid substitution as suggested by Scott, since these references as cited above indicate that the number of ice contact points is the limiting factor in anti-freeze activity. Thus, increasing the number of ice contact points by the addition of AFP repeat sequences (note the same conclusion was admitted by appellants from a review of Chakrabartty (19) and Scott, see page 12, last paragraph, ending on page 13 of the specification), or adding ice contact points via amino acid substitution, or using like amino acids instead of the naturally occurring ones were all suggested by the prior art to enhance AFP

Appeal No. 94-3056
Application 07/812,421

activity, and the art provides both the motivation and a reasonable expectation of enhanced AFPs.

We do not agree that "adding additional repeat sequences" is reasonably "suggested by Chakrabartty", nor that Chakrabartty and Scott "indicate that the number of ice contact points is the limiting factor in antifreeze activity." The examiner argues that Chakrabartty teaches length variation in the right hand column of page 11315. See page 11 of the Final Rejection and page 8 of the Appeal Brief. We find that Chakrabartty there refers to "analogs which vary in length" in the context of "repeating the experiment". Chakrabartty's work involves analogs of 1 repeat, 2 repeats and 3 repeats. See Table 1 of Chakrabartty on page 11314. The reference does not teach lengthening the polypeptide by adding more than three repeats. The polypeptides of claims 32-37 contain six or eight specified 11-amino acid sequence "repeats". Polypeptides of this length with this number of repeats are neither taught by nor reasonably suggested by the teachings of Chakrabartty. Nor is a finding that the limiting factor in antifreeze activity is the "number of ice contact points"

Appeal No. 94-3056
Application 07/812,421

reasonably supported by the Chakrabartty and Scott teachings. These references note the significance of the number of ice contact points, but they do not lessen the significance of other factors, including the known number of contiguous repeats in known antifreeze polypeptides.

Hindsight shall not form the basis of a conclusion of obviousness under 35 U.S.C. § 103. "Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure." In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). The prior art of record does not denominate the critical features of appellants' invention; i.e. proteins containing the six-repeat and eight-repeat sequences required by claims 32-37. As the Federal Circuit stated in Sensonics, Inc. v. Aerosonic Corp.,

81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996):

To draw on hindsight knowledge of the patented invention, when the prior art does not contain or suggest that knowledge, is to use the invention as a template for its own reconstruction - an illogical and inappropriate process by which to determine patentability. . . . The invention must be viewed not after the blueprint has been drawn by the inventor, but as it would have

Appeal No. 94-3056
Application 07/812,421

been perceived in the state of the art that
existed at the time the invention was made.
[citations omitted]

Thus, we hold that claims 32-37 define polypeptides which
would not have been obvious in view of the prior art cited by
the examiner.

New Rejection under the provisions of 37 CFR § 1.196(b)

Claim 37 is rejected under 35 U.S.C. § 112, second
paragraph.

Claim 37 is indefinite in the recitation of "a protein
expressed from" the specified plasmid. In addition to the
double fusion protein (P10:WF8R:\$-gal) described at pages 21-
24 of the
specification, from which the antifreeze polypeptide WF8R (SEQ
ID NO:2 shown in Figure 4) can be extracted, plasmid pGX28L
contains at least one other gene which encodes a protein. The
commercially available starting plasmid pGEM3Z(+) contains a
structural gene for a protein that is used in screening the
transformed *E. coli* for positive clones, i.e. those bacteria
which have taken up the desired plasmid. This gene is
referred to throughout Figures 9a-9c as "amp^R". This gene is
present in pGX28L, ATCC deposit No. 68425, as is shown in the

Appeal No. 94-3056
Application 07/812,421

depiction of this plasmid in Figure 9c. It is well known that the protein expressed from "amp^R" is β -lactamase, which cleaves the lactam ring of the antibiotic ampicillin. Transformed *E. coli* survive the addition of ampicillin to the culture medium while untransformed *E. coli* die upon addition of the ampicillin antibiotic to the culture medium. Thus, the specified protein is capable of expressing the β -lactamase protein as well as the double fusion protein referred to in the specification as p10:WF8R: β -gal.

As set forth in In re Zletz, 893 F.2d.319, 321-322, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989)(citations omitted):

...during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed. . . . An essential purpose of patent examination is to fashion claims that are precise, clear, correct and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.

In our view, claim 37 encompasses at least one protein which appellants do not regard as their invention. Clarification of the claim is required.

CONCLUSION

Appeal No. 94-3056
Application 07/812,421

We reverse the rejection of claims 32-37 under 35 U.S.C. § 103.

We newly reject claim 37 under 35 U.S.C. § 112, second paragraph, and the provisions of 37 CFR § 1.196(b).

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

REVERSED; 37 CFR § 1.196(b)

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WILLIAM F. SMITH)	
Administrative Patent Judge)	
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Administrative Patent Judge)	APPEALS AND
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Appeal No. 94-3056
Application 07/812,421

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