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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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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 HANSJORG TREICHLER, KENJI TAKABAYASHI,
DIETER H. WOLF and JUTTA HEIM

Appeal No. 1995-2518
Application 07/895,581¹

ON BRIEF

Before WILLIAM F. SMITH, ELLIS, and ROBINSON, Administrative Patent Judges.

ROBINSON, 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 51 - 61, which are all of the claims pending in this application.

¹ Application for patent filed June 8, 1992. According to appellants, this application is a continuation of Application No. 07/346,670, filed May 3, 1989, now abandoned.

An understanding of the invention can be derived from a reading of claims 51, 52, and 53, which are reproduced below:

51. A *Saccharomyces cerevisiae* strain which lacks carboxypeptidase ysc" activity and lacks proteolytic activity selected from the group consisting of proteolytic yscA, yscB, yscY and yscS activity and has been transformed with a hybrid vector comprising a *Saccharomyces cerevisiae* promoter operably linked to a DNA coding for a full-length mature protein which bears no basic C-terminal amino acids and which is selected from the group consisting a hANP, EGF, connective tissue activating peptide-III and desulphatohirudin.

52. A method for the production of a *Saccharomyces cerevisiae* strain which lacks carboxypeptidase ysc" activity and lacks proteolytic activity selected from the group consisting of proteolytic yscA, yscB, yscY and yscS activity and has been transformed with a hybrid vector comprising a *Saccharomyces cerevisiae* promoter operaly linked to a DNA coding for a full-length mature protein which bears no basic C-terminal amino acids and which is selected from the group consisting of hANP, EGF, connective tissue activating peptide-III and desulphatohirudin, comprising transforming a *saccharomyces cerevisiae* strain which lacks carboxypeptidases ysc" activity and lacks proteolytic activity selected from the group consisting of proteolytic yscA, yscB, yscY and yscS activity with said hybrid vector.

53. A method for the production of a full-length mature protein which bears no basic C-terminal amino acids and which is selected from the group consisting of hANP, EGF, connective tissue activating peptide-III and desulphatohirudin, comprising culturing a *Saccharomyces cerevisiae* strain which lacks carboxypeptidase ysc" activity and lacks proteolytic activity selected from the group consisting of proteolytic yscA, yscB, yscY and yscS activity and has been transformed with a hybrid vector comprising a *Saccharomyces cerevisiae* promoter operably linked to a DNA coding for said protein, and isolating said protein.

The references relied upon by the examiner are:

Bussey et al. (Bussey)	4,929,553	May 29, 1990
Hinnen et al. (Hinnen)	EPA 0,213,593	Mar. 11, 1987
Meyhack et al. (Meyhack)	EPA 0,225,633	Jun. 16, 1987

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Achstetter et al. (Achstetter), "Proteinases, Proteolysis and Biological Control in the Yeast *Saccharomyces cerevisiae*," Yeast, Vol. 1, pages 139-157, 1985

Strathern et al. (Strathern), The Molecular Biology of the Yeast *Saccharomyces*. Life Cycle and Inheritance, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, page 458, 1981.

Kingsman et al. (Kingsman), "Heterologous Gene Expression in *Saccharomyces cerevisiae*," Biotechnol. Genet Engr. Rev., Vol. 3, pages 377-416, 1985.

Grounds of Rejections

Claims 51-55 and 57-61 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Bussey, Achstetter, Hinnen and Meyhack.

Claim 56 stands rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Bussey, Achstetter, Hinnen, Meyhack and Strathern.

Claim 57 stands rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Bussey, Achstetter, Hinnen, Meyhack and Kingsman.

We reverse.

BACKGROUND

At pages 1, 3 and 4 of the specification, the applicants describes the invention as relating to an improved method for the production of a protein heterologous to yeast in a homogeneous form by culturing a yeast strain which lacks carboxypeptidase ysc" activity and has been transformed with a hybrid vector comprising a yeast promoter operably linked to a DNA sequence coding for the heterologous protein and isolating said

heterologous protein. The preferred yeast strain is also described as being defective in at least one protease activity selected from yscA, yscB, yscY and yscS which serves to further reduce random proteolysis of the protein product. The invention is said to include the process of producing the protein, the genetically engineered yeast cells and the methods of preparing the yeast cells.

Discussion:

Claims:

Claim 51 is directed to a *Saccharomyces cerevisiae* strain which lacks carboxypeptidase ysc" acid and lacks proteolytic activity selected from the group consisting of proteolytic yscA, yscB, yscY and yscS. The strain has been transformed with a hybrid vector comprising a *S. cerevisiae* promotor operably linked to a DNA which will encode a full-length mature protein having no basic C-terminal amino acids wherein the protein is selected from the group consisting of hANP, EGF, connective tissue activating peptide-III and desulphatorhirudin. Claim 52 is directed to a method of producing a *S. cerevisiae* strain claimed in claim 1 and claim 53 is directed to a method of producing a full-length mature protein using a *S. cerevisiae* strain claimed in claim 1.

The rejections under 35 U.S.C. § 103

Claims 51-55 and 57-61 stand rejected under 35 U.S.C. § 103 as being unpatentable over Bussey taken with Achstetter, Hinnen and Meyhack.

Claim 56 stands rejected under 35 U.S.C. § 103 as being unpatentable over

Bussey taken with Achstetter, Hinnen, and Meyhack in further view of Strathern.

Claim 57 stands rejected under 35 U.S.C. § 103 as being unpatentable over

Bussey taken with Achstetter, Hinnen, and Meyhack in further view of Kingsman.

We have chosen to group the grounds of rejection before us under 35 U.S.C. § 103, since all three rejections depend on the examiner's consideration of Bussey, Achstetter, Hinnen and Meyhack. Appellants have argued the separate rejections of claim 56 and 57 only to the extent that it is urged that the rejection of these claims should fail for the same reasons advanced relative to the first rejection. (Principal Brief, page 8).

In describing Bussey, the examiner states (Answer, page 4):

Bussey *et al.* disclose strains of *S. cerevisiae* with a null mutation of the KEX1 gene (col 3) obtained by gene disruption (col 6, lines 6-11) so that it allows for the production of desired protein precursors retaining the C-terminal residues (col 6, lines 20-27). While Bussey *et al.* do not explicitly disclose the additional yscA, yscB, yscY and yscS proteolytic activities, Bussey *et al.* nevertheless set forth the teaching of producing proteins where the C-terminal is intact and the post translational processing can be tailored as Bussey *et al.* disclose that the processing can be carried out *in vitro* to process the selected secreted proteins which means that the heterologous protein is obtained from the transformed yeast with the C-terminal intact and unmodified and a yeast without an active ysc" gene would not have been expected to have an active ysc" gene product

The examiner relies on Achstetter as disclosing (Answer, page 4):

[t]he isolation of yeast strains in which the genes coding for yscA, B, Y, and S contain mutations (pages 141-142 and 145) and which also teaches that proteinase yscB deficiency results in a decrease in protein degradation of 40-60%. . .

The examiner concludes that (Answer, page 4):

[o]ne of ordinary skill in the art would have found it obvious to modify the teachings in the Bussey *et al.* reference by applying the teachings of the Achstetter *et al.* reference to construct a mutant yeast which was deficient in the production of ysc" and one or more of yscA, yscB, yscY and yscS proteolytic activities such as by gene disruption disclosed in the Bussey *et al.* reference or any other art recognized routine technique with the expectation of having a strain of yeast with decreased protein degradation of at least 40-60% as taught in the reference.

Both Hinnen and Meyhack are relied upon as teaching the transformation of yeast with hybrid vectors for the expression of heterologous proteins of the type designated in the claims. (Answer, page 5).

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). We have carefully considered the evidence and discussion in support of the rejection presented by the examiner. However, we feel that a fair evaluation of the references, applicants' specification and consideration of the claimed subject matter as a whole, dictates a conclusion that the construction of the claimed subject matter from the prior art teachings is not suggested by the record before us. To establish a prima facie case of obviousness, there must be more than the demonstrated existence of all of the components. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge can not come from the applicants' invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675,

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678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). The extent to which such suggestion must be explicit in or may be fairly inferred from, the references, is decided on the facts of each case, in light of the prior art and its relationship to the invention. It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed inventions using applicants' claimed invention as a template and selecting elements from references to fill the gaps. In re Gorman, 933 F.2d 983, 986-987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). We find no reasonable suggestion for combining the genetic characteristics of the *S. cerevisiae*, which lack proteolytic yscA, yscB, yscY or yscS activity, as described by Achstetter with the genetic altered *S. cerevisiae* of Bussey to arrive at a strain of which lacks both carboxypeptidase ysc" activity and at least one proteolytic activity selected from yscA, yscB, yscY and yscS.

The examiner has proposes that, if the combination of the two genetic traits of Bussey and Achstetter were combined into a single strain of Sc, one skilled in the art would have had a reasonable expectation of success of obtaining the *S. cerevisiae* useful in the manner claimed. In re O'Farrell, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). However, in addition to "a reasonable expectation of success" there must also be a reason, suggestion or motivation to combine the teachings of the prior art in the first place. In re O'Farrell, 853 F.2d at 902, 7 USPQ2d at 1680. The examiner urges that one

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skilled in the art would have been so motivated (Supplemental Answer, page 3):

[t]o further minimize the effects of inadvertent processing and maximize heterologous protein production one of ordinary skill in the art would have found it obvious to combine the teachings of Bussey et al. with that of Achstetter et al. . . .

However, the examiner does not indicate where in the prior art, relied upon, such a need is suggested. Patentability should be based on a comparison of the claimed subject matter and the prior art. It is the prior art which must provide some basis for combining the relevant disclosures and it is improper for the examiner to substitute the skill in the art for prior art, rather than using the skill in the art to interpret the prior art. In re Kratz, 592 F.2d 1169, 1175, 201 USPQ 71, 76 (CCPA 1979).

The remaining references, Hinnen, Meyhack, Strathern, and Kingsman, do not provide the reason, suggestion or motivation determined to be missing and necessary to support the combination of the disclosures of the previously discussed references.

Therefore, with regard to claims 51-61, it is our conclusion that the examiner has failed to establish a prima facie case of unpatentability of the claimed subject matter.

The rejections under 35 U.S.C. § 103 are reversed.

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Summary

We reverse the rejections of claims 51-61 under 35 U.S.C. § 103.

REVERSED

WILLIAM F. SMITH)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
JOAN ELLIS)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
)	
DOUGLAS W. ROBINSON))	
Administrative Patent Judge)	

DWR/pgg
Michael W. Glynn
Novartis Corporation

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564 Morris Avenue
Summit, NJ 07901