

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 23

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte CHARLES P. HART

Appeal No. 1995-4717
Application 07/876,288¹

ON BRIEF

Before METZ, ELLIS, and ROBINSON, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 7 and 24, which are all of the claims pending in this application.

A copy of the appealed claims are appended to this decision.

¹ Application for patent filed April 29, 1992.

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The references relied upon by the examiner are:

Cronan WO 90/14431 November 29, 1990

Devlin et al. (Devlin), "Random Peptide Libraries: A Source of Specific Protein Binding Molecules," Science, vol. 249, pp. 404-406, 1990.

Scott et al. (Scott), "Searching for Peptide Ligands with an Epitope Library," Science, vol. 249, pp. 386-390, 1990.

Maina et al. (Maina), "An *Escherichia coli* Vector to Express and Purify Foreign Proteins by Fusion to and Separation from Maltose Binding Protein," Gene, vol. 74, pp. 365-373, 1988.

Plückthun et al. (Plückthun), "The Rationality of Random Screening-Efficient Methods of Selection of Peptides and Oligonucleotide Ligands," Angew. Chem. Int. Ed. Engl., vol. 30, no. 3, pp. 296-298, 1991.

Berg, "Zinc Fingers and Other Metal-Binding Domains," The Journal of Biological Chemistry, vol. 265, no.12, pp. 6513-6516, 1990.

O'Neil et al. (O'Neil), "Design of DNA-Binding Peptides Based on Leucine Zipper Motif," Science, vol. 249, pp. 774-778, 1990.

GROUND OF RECORD

Claims 2 through 7 stand rejected under 35 U.S.C. § 112, second paragraph, as failing to particularly point out and distinctly claim the invention.

Claims 1 through 5 and 24 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Devlin, Cronan, Scott, Maina, and Plückthun.

Claims 6 through 7 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Devlin, Cronan, Scott, Maina, Plückthun, Berg, and O'Neil.

We reverse.

BACKGROUND

The invention is described at pages 3-4 of the specification as being directed to a method of generating a random peptide library wherein host cells are transformed with a set of recombinant DNA vectors that code for the expression of a tripartite fusion protein made up of a carrier protein, a peptide, and a proteolytic cleavage site between the carrier protein and the peptide. The transformed host cells are then cultured under conditions suitable for expression of the fusion protein. The peptide library is said to be useful in the identification of peptides that bind to receptor molecules of interest.

DISCUSSION

The Claims:

Claim 1 is directed to a two step method of generating a random peptide library. The initial step comprises transforming host cells with a set of recombinant DNA vectors. Each vector encodes a different tripartite fusion protein which consists essentially of a carrier protein, a peptide and a proteolytic cleavage site. The vectors differ from one another with respect to the peptide encoded. The peptide portion of the fusion protein can be "specified exactly, completely random, composed of the production of building variation around a core or lead sequence, either immobilized or a free peptide, or presented in a

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molecular scaffolding structure." (Specification, page 12). The second step of the claimed method requires the culturing of the transformed host cells under conditions suitable for expression of the fusion protein. Claim 6 provides that the peptide is comprised of amino acid residues that introduce conformation constraints on the peptide. Claim 24 provides for a secondary library wherein the peptide of the tripartite fusion protein is a variation of a lead peptide sequence.

The rejection under 35 U.S.C. § 112, second paragraph

Claims 2 through 7 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The examiner states that the phrase "where n is at least 3" (claim 2) fails to set forth a closed limit in the number of members of the Markush group in which it appears and therefore the number of members is indefinite (Answer, page 6). In determining whether claim language runs afoul of the second paragraph of 35 U.S.C.

§ 112, we must analyze the definiteness of the language employed in claims not in a vacuum, but always in light of the teachings of the prior art and the application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. In re Sneed, 710 F.2d 1544, 1548, 218 USPQ 385, 388 (Fed. Cir. 1983); In re Angstadt, 537 F.2d 498, 501, 190 USPQ 214, 217 (CCPA 1976). The claims are deemed definite so long as they reasonably apprise one of ordinary skill in the art of their scope. In re

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Warmerdam, 33 F.3d 1354, 1361, 31 USPQ2d 1754, 1759 (Fed. Cir. 1994). In claim 2, the protein represented by His_n serves as the carrier protein as part of the fusion protein. For any value of "n", one skilled in this art could readily determine whether the substance represented by "His_n" will serve as a carrier protein and thus does or does not fall within the scope of the claims. That the phrase appears in a Markush group does not serve as a basis to evaluate it in a different manner. We therefore reverse the rejection of claims 2 through 7 under 35 U.S.C. § 112, second paragraph.

The rejections under 35 U.S.C. § 103

Claims 1 through 5 and 24:

Claims 1 through 5 and 24 stand rejected under 35 U.S.C. § 103 as being unpatentable over Devlin in view of Cronan, Scott, Maina and Plückthun.

In describing the reliance on Devlin, the examiner states (Answer, paragraph bridging pages 6-7):

Devlin et al. disclose the production of random peptide libraries in both 8gt11 and in filamentous phage (see e.g. page 404, first column, second paragraph, lines 3-9 and lines 15-19). These random, semi-representative libraries comprised 15 residue peptides made by transforming host cells with vectors containing random peptide coding sequences and culturing the resultant transformed cells.

The examiner acknowledges (Answer, page 7) that Devlin does not disclose the use of vectors encoding tripartite fusion proteins in the construction of the disclosed library, but relies upon Cronan (Answer, page 7) as disclosing a tripartite fusion protein vector which has a cleavage site, exemplified by Factor Xa, which results in expression of the

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protein in either the cytoplasm or the periplasm of E. coli. Cronan is also relied upon as teaching that the fusion protein with a cleavage site would have allowed one to purify a protein of interest, for example using affinity chromatography targeted towards the fusion protein partner, and to subsequently cleave the purified protein from the fusion protein partner at the cleavage site. Scott is cited (Answer, pages 7-8) as disclosing the use of binding protein for screening random peptide libraries. Maina is cited as disclosing (Answer, page 8) the use of E. coli vectors to express and purify foreign fusion proteins and specifically exemplifies maltose binding protein as useful for this purpose. Finally, Plückthun is relied upon for the disclosure that (Answer, page 7) "general solutions of finding optimal ligands . . . will . . . be carried out outside the cell." The examiner then concludes (Answer, pages 8-9):

As illustrated by the cited prior art, it was generally recognized that generating libraries of a random or semi-random nature would have been useful for a variety of purposes; for example, in elaborating the structure of ligands of receptors or antibodies. Since the art recognized the concept of using expression of random peptides in heterologous systems such a bacteria, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the expression vectors of Cronan et al. to express random recombinant peptides because these vectors were taught to be advantageous for purification and analysis of recombinantly produced proteins. Many methods were available for generating recombinant, random peptide libraries and the particular choice of vectors as claimed was known at the time of 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). On the record before us, we find that the examiner has failed to establish a prima facie case of unpatentability of the claimed subject matter.

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To establish a prima facie case of obviousness, there must be more than the demonstrated existence of all of the components of the claimed process. There must be some reason, suggestion, or motivation found, implicitly or explicitly, in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. One can not substitute the skill in the art for a teaching in the prior art. In re Kratz, 592 F.2d 1169, 1175, 201 USPQ 71, 76 (CCPA 1979). Also, that knowledge can not come from the applicant's invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 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). It is impermissible to engage in a hindsight reconstruction of the claimed invention using applicant's 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, motivation, or direction in the prior art relied upon by the examiner, which would have lead one of ordinary skill in this art to generate random peptide libraries using a carrier protein-cleavage site-random protein construct, as claimed. We conclude that the examiner has failed to establish a prima facie case of unpatentability of the claimed subject matter. 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, therefore, reverse the rejection of claims 1-6, 9 and 10

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under 35 U.S.C. § 103.

Claims 6 and 7:

In the rejection of claims 6 and 7 under 35 U.S.C. § 103 the examiner relies on the references discussed above, taken in further combination with Berg or O'Neil. In view of our determination regarding the previous rejection, it is only necessary to determine whether Berg or O'Neil provide that which is missing from the other references. They do not. "Berg discloses the primary amino acid sequence and structure of the zinc finger containing peptides" (Answer, page 9) and "O'Neil et al. disclose the design of DNA-binding peptides wherein said peptides include leucine zipper motifs" including "the sequence of particular peptides that form leucine zippers . . . and the overall repeating structure of leucine zipper containing peptides." (Answer, paragraph bridging pages 9-10). However, neither reference provides the reason, suggestion or motivation determined to be missing and necessary to support the combination of the disclosure of the previously discussed references. Therefore, with regard to claims 6 and 7, we conclude that the examiner has failed to established a prima facie case of unpatentability of the claimed subject matter. The rejection of claims 6 and 7 under 35 U.S.C. § 103 is reversed.

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CONCLUSION

The examiner's rejection of claims 2 through 7 under 35 U.S.C. § 112, second paragraph, is reversed.

The examiner's rejection of claims 1 through 5 and 24 under 35 U.S.C. § 103 is reversed.

The examiner's rejection of claims 6 and 7 under 35 U.S.C. § 103 is reversed.

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

REVERSED

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ANDREW H. METZ)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
JOAN ELLIS)	
Administrative Patent Judge)	APPEALS AND
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