

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte

BRUCE A. GREEN AND GARY W. ZLOTNICK

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Appeal No. 1999-1313  
Application No. 08/448,097

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ON BRIEF

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

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 28-30, 38-46, 81-83, and 88, all of the claims remaining in this application.

Claims 28, 38, and 88 are exemplary of the claims on appeal, and read as follows:

28. Isolated nucleic acid encoding essentially pure protein “e” of Haemophilus influenzae or a peptide of protein “e” comprising an epitope or epitopes thereof.

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38. A recombinant cloning or expression vector containing nucleic acid encoding essentially pure protein "e" of Haemophilus influenzae or a peptide of protein "e" comprising an epitope or epitopes thereof.

88. A method of producing essentially pure protein "e" of Haemophilus influenzae which comprises transforming, transducing or transfecting an infectious microorganism with the vector of Claim 38 and culturing the infectious microorganism under conditions which permit the expression of said protein "e" by the infectious microorganism.

The examiner relies on the following references:

Granoff et al (Granoff) "Prospects for the Prevention of Hemophilus influenzae Type b Disease by Immunization, The Journal of Infectious Diseases, vol 153, no.3 pp 448-461, March 1986

Deich et al (Deich), "Cloning of genes encoding 15,000-Dalton Peptidoglycan-Associated Outer membrane Lipoprotein and an Antigenically Related 15,000-Dalton Protein from Haemophilus influenzae," Journal of Bacteriology vol.170 no2, pp 489-498, February 1988

Maniatis et al (Maniatis) Molecular Cloning: A Laboratory Manual, Editor: Sambrook, Fritsch, Maniatis, vol. 2-3 1989.

In the Examiner's Answer, page 2, § 10, the examiner withdrew a previously entered rejection of claims under 35 U.S.C. 112, 1st paragraph. The sole issue remaining on appeal is whether the examiner erred in rejecting claims 28-30, 38-46, 81-83, and 88 under 35 U.S.C. 103 as unpatentable over the combined disclosures of Granoff, Deich, and Maniatis.

We reverse.

#### BACKGROUND

Nontypable Haemophilus influenzae cause diseases in adults, children, and young adults (specification, page 1). Antiserum directed against the capsular polysaccharide of

H. influenza type B is bactericidal and protective against H. influenzae type B, but is ineffective against nontypable H. influenzae (specification, page 2). A lipoprotein found in the outer membrane of H. influenzae, having a molecular weight of about 28,000 daltons, is designated protein "e" (specification, page 2). The same protein is designated P4 in Granoff (Examiner's Answer, page 3). The invention pertains to nucleic acids encoding this protein, and to nucleic acids encoding peptides and proteins having an epitope in common with protein "e", and to recombinant methods of producing protein "e" (specification, pages 2-5). In the parent application, claims have been patented, essentially drawn to a vaccine composition comprising essentially pure protein "e" of Haemophilus influenzae or a peptide of protein "e" comprising an epitope or epitopes thereof, in a pharmaceutically acceptable vehicle; wherein the protein "e" of Haemophilus influenzae or the peptide of protein "e" elicits a protective immune response in a mammalian host (see claim 1 of U.S. 5,601,831, matured from Application No. 07/491,466).

#### Discussion

The initial burden of establishing unpatentability rests on the examiner. In re Oetiker, 977 F. 2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed

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composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. In re Vaeck, 947 F.2d. 488, 495, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). The examiner must show that some objective teaching or suggestion in the applied prior art, or knowledge generally available in the art, would have led one of ordinary skill in the art to the claimed invention. Pro-Mold & Toll Co. v. Great Lakes Plastics, Inc., 75 F. 3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed. Cir. 1996).

In reaching our decision in this appeal, we have given careful consideration to appellants' specification and claims and to the respective positions articulated by appellants and the examiner. We make reference to the Examiner's Answer mailed June 24, 1998 (Paper No. 16 ) for the examiner's reasoning in support of the rejection, and to the Appeal Brief, received March 2, 1998 (Paper No. 15), and Reply Brief, received October 29, 1998 (Paper No. 18) for appellants' arguments against the rejection. We have also carefully considered the references cited by the examiner.

In rejecting the appealed claims, the examiner characterizes Granoff as teaching the purification of a 28 KD protein from H. influenzae, termed P4, which is the same as appellant's protein "e". The examiner cites Deich as teaching the cloning and

characterization of DNA from H. influenzae, and Maniatis as teaching routine procedures of expressing proteins in host cells. The examiner states that

“One of ordinary skill in the art would have been motivated to make such DNAs [encoding “e”] because of the unique properties of the Hemophilus influenza proteins in that such proteins can be used as diagnostic markers and/or vaccine candidates for infections caused by Hemophilus influenza, reagents to raise antibodies for detection or diagnostic assays, and the technique of generating recombinant proteins by expressing DNA would have allowed for the ability to obtain large quantities of proteins.”

Examiner’s Answer, page 3.

Appellants do not dispute that Granoff teaches a purified protein P4, which is the same as protein “e”. However, appellants argue that, due to improper purification methods, Granoff was unable to obtain essentially purified protein “e” which would have utility in a vaccine. Appellants further argue that a fair reading of Granoff would have led a person of ordinary skill in the art to conclude that protein “e” (P4) was not a viable vaccine candidate, and would have been dissuaded from attempting to obtain the gene encoding protein “e”. We agree.

We find that Granoff does not provide adequate reason, suggestion, or motivation to choose the P4 protein for cloning. Although a person having ordinary skill in the art might be generally motivated to use H. influenzae proteins as diagnostic markers and/or vaccine candidates, or as reagents to raise antibodies for detection or diagnostic assays, nonetheless, Granoff does not provide adequate suggestion that the P4 protein would be useful for these purposes. Granoff teaches that antisera to purified P4 protein does not

provide protection against bacteremia, and that epitopes of P4 were not detectable at the cell surface. Therefore the reference provides inadequate reason, suggestion, or motivation to choose this particular protein for further work, and we agree with appellants that one of ordinary skill would have been dissuaded from attempting to obtain the gene encoding protein "e". The examiner further argues, in rebuttal to the arguments advanced in the brief, that "the nucleic acids encoding claimed proteins or fragments can be used as probes in hybridization assays," (Examiner's Answer, page 5). However, the examiner does not point to any reason, suggestion, or motivation, stemming from the prior art, which would have led a person having ordinary skill to select the P4/"e" protein coding sequence for this purpose.

We conclude that the examiner has not met the initial burden of establishing unpatentability. The examiner's decision, rejecting claims 28-30, 38-46, 81-83, and 88 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

Sherman D. Winters  
Administrative Patent Judge

William F. Smith

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