

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 27

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte CHARLES W. RITTERSHAUS

Appeal No. 2000-1812
Application No. 08/432,483

HEARD: November 27, 2001

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

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2, 5 - 8, 10 - 12, 14 - 18, and 27 - 29, which are all of the claims pending in the application.

Claims 1, 2, 5, and 11 are illustrative of the subject matter on appeal and read as follows:

1. An isolated antigenic hybrid peptide comprising a helper T cell epitope portion linked to a B cell epitope portion, wherein said B cell epitope portion comprises six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesteryl ester transfer protein (SEQ ID NO: 1).

Grounds of Rejection

Claims 1, 2, 6 - 8, and 27 stand rejected under 35 U.S.C. § 103¹. As evidence of obviousness, the examiner relies on Swenson and Valmori.

Claims 1, 2, 5 - 8, 10, and 27 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Swenson, Valmori and Weiner.

Claims 1, 2, 5 - 8, 10 - 12, 14 - 18, and 27 - 29 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Swenson, Valmori, Weiner, and Whitlock .

We reverse for reasons set forth herein.

Discussion

In reaching our decision in this appeal, we have given careful consideration to the appellant's specification and claims and to the respective positions articulated by the appellant and the examiner. We make reference to the Examiner's Answer of April 26, 1999 (Paper No. 21) for the examiner's reasoning in support of the rejections and to the appellant's Appeal Brief, filed January 28, 1999 (Paper No. 20) and Reply Brief filed June 30, 1999 (Paper No. 23)², for the appellant's arguments thereagainst.

¹ The examiner has withdrawn the rejection of claim 5 under this rejection. (Answer, page 6).

² In the Office action of September 9, 1999 (Paper No. 24), the examiner noted the entry and consideration of the Reply Brief but indicated that no further response was necessary. In addition to arguments, appellant included, as evidence, an article by Michel which had not previously been addressed by the Examiner on this record. Having entered the Reply Brief and thus the arguments relating to this evidentiary article and having

(continued...)

Background

As background to this invention the applicant, at pages 2-4 of the specification explains that it is known that cholesteryl ester transport protein (CETP) is known to mediate the transfer of cholesteryl esters from high density lipoproteins (HDL) to triglyceride-rich lipoproteins such as very low density lipoproteins (VLDL) and low density lipoproteins (LDL) and also the reciprocal exchange of triglycerides from VLDL to HDL. It is suggested that CETP may play a role in modulating the levels of cholesteryl esters and triglycerides associated with various classes of lipoproteins. It has apparently been established that a high CETP cholesteryl ester transfer activity has been correlated with increased levels of LDL-associated cholesterol and VLDL-associated cholesterol which is in turn correlated with increase risk of cardiovascular disease. Similarly, decreased susceptibility to cardiovascular disease, such as atherosclerosis is generally correlated with increased absolute levels of circulating HDL and increased levels of HDL relative to circulating levels of lower density lipoproteins such as VLDL and LDL. Thus, applicant explains that increased levels of cholesteryl ester transfer activity can produce a decrease in HDL levels relative to LDL and VLDL levels which is correlatable with an increased risk of atherosclerosis. Appellant describes the claimed invention at page 6 of the Specification as being directed to compounds and methods useful for modulation or inhibition of cholesteryl ester transfer protein activity, using vaccine peptides which when

²(...continued)
maintained the all grounds of rejection, it is can be presumed that the examiner did not find either the arguments or additional evidence persuasive of error in the rejections presented in the Examiner's Answer.

administered to a mammal raise an antibody response against the mammal's own endogenous CETP. These peptides are described as being comprised of a helper T cell epitope portion linked to a B cell epitope portion comprised of all or a portion of the carboxyl terminal portion of human CETP protein.

Claim Interpretation

Claim 1 is directed to an isolated antigenic hybrid peptide comprising a T cell epitope portion linked to a B cell epitope portion wherein the B cell epitope comprises six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesteryl ester transfer protein. This 26 amino acid sequence is defined in SEQ ID NO: 1 of the specification. Claim 2 is directed to the isolated antigenic hybrid peptide but further provides that the T cell epitope portion is selected from a defined group which includes tetanus toxoid, among other T cell epitopes. Claim 5 is directed to an isolated antigenic hybrid peptide comprising the amino acid sequence of SEQ ID NO: 2. As noted by the examiner (Answer, page 8) "[c]laim 5 is not limited to conjugates consisting of just the 16 amino terminal residues of CETP." The use of the term comprising in claim 5 opens up the claim to read upon a peptide comprising the 16 mer but also containing additional CETP residues. Claim 11 is directed to a method of elevating the ratio of circulating HDL to circulating LDL, VLDL or total cholesterol in an animal or human by administering to the animal or human an antigenic vaccine hybrid peptide of the type claimed in claim 1. Claim 29 is directed to a method of treating atherosclerosis in a

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human or animal by administering thereto a vaccine hybrid peptide comprising a universal helper T cell epitope portion linked to a B cell epitope portion wherein the B cell epitope portion comprises six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesteryl ester transfer protein.

The rejections under 35 U.S.C. § 103

The examiner's rejection of claims 1, 2, 6 - 8 and 27 depends on the combined teachings of Swenson and Valmori.

The examiner relies on Swenson as describing (Answer, page 3):

that CETP protein contains a B cell epitope localized to the 26-amino acid sequence at the carboxyl terminus to which a monoclonal antibody which neutralizes CETP activities binds. Swenson et al. Also teach a peptide with the same sequence and amino acid residues as SEQ ID NO: 1, see Peptide C in Table I. Thus, Swenson et al. teach a peptide with the exact length and amino acid residues of SEQ ID NO. 1.

The examiner acknowledges that Swenson does not teach the use of a hybrid peptide containing tetanus toxoid sequences in combination with amino acids from the terminal amino acid portion of CETP. (Id.).

The examiner cites Valmori as teaching that (Answer, page 4):

tetanus toxoid contains epitopes that are recognized by all primed donors irrespective of their MHC haplotypes. Valmori et al. also teach that tetanus toxoid peptide that are the same as amino acids 2-15 of SEQ ID NO. 2 and SEQ ID NO 3 (see page 717, in particular). Valmori et al. further teach that the tetanus toxoid T cell epitopes can be used as carrier (helper T cell epitopes) for B cell epitopes and that such hybrid peptides can be used to elicit antibodies in humans.

The examiner concludes that (Answer, page 5):

it would have been obvious to one of ordinary skill in the art at the time of the invention to make a CETP-toxoid hybrid peptide comprising amino acids sequences of the carboxyl terminal 26 amino acid of human CETP and the tetanus toxoid peptide taught by Valmori et al. including a peptide which consists of SEQ ID NO. 2 except that the cysteine is deleted with the expectation that such peptides would elicit anti-CETP antibody that binds to the known B cell epitopes in the C terminal end of CETP with the expectation that the antibodies would neutralize CETP activity. Alternatively the CETP-tetanus toxic hybrid peptide could be used in assays to screen for anti-CETP antibodies that neutralize CETP activity.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant. Id. In order to meet that burden the examiner must provide 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.), cert. denied, 475 U.S. 1017 (1986).

On the record before us, the examiner has not met the initial burden of establishing why the prior art, relied on, would have led one of ordinary skill in this art to arrive at an isolated antigenic hybrid peptide comprising a helper T cell epitope portion linked to a B cell portion wherein the B cell epitope portion comprises six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesteryl ester transfer protein. While it can reasonably be stated that Swenson describes raising antibodies in mice with

human cholesteryl ester transfer protein, and identifies and prepares certain monoclonal antibodies which bind to a portion of the 26 amino acid carboxyl terminus of CETP, as well as performing studies to evaluate the inhibitory effects on CETP activity when the monoclonal antibodies bind the CETP molecule, the reference does not provide a reason suggestion which would direct one of ordinary skill in this art to link any particular part of the CETP molecule with a T cell epitope such as those described by Valmori. It would reasonably appear that Swenson has successfully generated antibodies in mice using the intact CETP protein. Given Swenson's described success in generating one or more antibodies to CETP, there is nothing which would lead one to select a portion of the CETP molecule to be used in combination with a T cell epitope of Valmori for the purpose of generating additional antibodies. While Valmori might be read to suggest the use of T cell epitopes in combination with foreign antigens to assist in obtaining an antibody response in a human, there is nothing on this record which would reasonably suggest attempting to generate any type of immune response to CETP in a human. With regard to other animals, such as mice, Swenson already has a system which is demonstrated to be effective at generating antibodies in mice using the whole CETP protein and thus does not appear to need the assistance which would be provided by using the T cell epitopes provided by Valmori. Further, the examiner has provided no evidence which would reasonably suggest the incorporation of such an antigenic peptide into a vaccine composition as claimed in claims 6, 7, and 8.

Thus, the examiner has provided teachings relating to the components of the claimed invention which, if properly combined or modified, could be used to arrive at the

claimed invention. However, what is missing from the examiner's rejection of claims 1, 2, 6 - 8 and 27 is a teaching or suggestion to be found in the prior art which would have reasonably led those of ordinary skill in this art to the claimed invention. That Swenson and Valmori may, individually, describe components of the claimed invention, in the absence of evidence or facts which would reasonably suggest the modification of the explicit teaching of these references, would not have led one of ordinary skill to the claimed invention since the prior art does not suggest the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). In re Fritch, 972 F.2d 1260, 1266, n.14, 23 USPQ2d 1780, 1783-84, n.14 (Fed. Cir. 1982).

In the absence of such evidence, the only suggestion to prepare a hybrid peptide as presently claimed in claims 1, 2, and 27 and to incorporate such a peptide into a vaccine composition as claimed in claims 6, 7, and 8, is provided by appellant's disclosure of the invention. However, use of this information as a basis for establishing a prima facie case of obviousness, within the meaning of 35 U.S.C. § 103, would constitute impermissible hindsight. 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 modifications required. 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). Thus, on this record, the examiner has not provided those facts or evidence which would reasonably support a conclusion that the claimed subject matter would have been

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prima facie obvious within the meaning of 35 U.S.C. § 103. 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). Therefore, the rejection of claims 1, 2, 6 - 8 and 27 under 35 U.S.C. § 103 is reversed.

The examiner's rejection of claims 1, 2, 5 - 8, 10 and 27 as unpatentable over the combined teachings of Swenson, Valmori and Weiner, as well as the rejection of claims 1, 2, 5 - 8, 10 - 12, 14 -18, and 27 - 29 as unpatentable over the combined teaching of Swenson, Valmori, Weiner, and Whitlock, rest principally on the evidentiary basis provided by the combination of Swenson and Valmori. Having determined that Swenson and Valmori, taken in combination, would not have provided sufficient basis for rejecting claims 1, 2, 6 - 8 and 27, consideration of the remaining two rejections requires only that we determine whether either Weiner or Whitlock, alone or in combination, provide that which is missing from the combination of Swenson and Valmori.

Weiner does not relate the CETP and is relied on by the examiner only to demonstrate that "amino terminal cysteine added to sequence of peptides during synthesis allows the coupling of the peptide to proteins . . ." (Answer, page 7). Whitlock, like Swenson, describes studies relating to CETP where an antibody was used to neutralize CETP activity. (Answer, page 8). As with Swenson, Whitlock provides no teaching which would reasonably be read to lead those of ordinary skill in this art to modify the CETP described therein by combining all or a portion of the CETP molecule with a T

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cell epitope of the type taught by Valmori in a manner which would result in the claimed antigenic peptide. Thus, Weiner and Whitlock do not provide that which we have determined to be missing from the combination of Swenson and Valmori. We therefore, reverse the remaining two grounds of rejection under 35 U.S.C. § 103.

Summary

The rejection of claims 1, 2, 6 - 8, and 27 under 35 U.S.C. § 103 as unpatentable over the combined teachings of Swenson and Valmori is reversed. The rejection of claims 1, 2, 5 - 8, 10, and 27 under 35 U.S.C. § 103 as unpatentable over the combined teachings of Swenson, Valmori, and Weiner is reversed. The rejection of claims 1, 2, 5

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- 8, 10 - 12, 14 - 18 and 27 - 29 under 35 U.S.C. § 103 as unpatentable over the combined teachings of Swenson, Valmori, Weiner and Whitlock is reversed.

REVERSED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
)	
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)	BOARD OF PATENT
DOUGLAS W. ROBINSON)	
Administrative Patent Judge)	APPEALS AND
)	
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