

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte TSE W. CHANG, MICHAEL S. C. FUNG, BILL N. C. SUN,
CECILY R. Y. SUN and NANCY T. CHANG

Appeal No. 1997-2392
Application No. 08/089,990

ON BRIEF

Before WINTERS, SCHEINER, and ADAMS, Administrative Patent Judges.

ADAMS, 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, 4, 5 and 7, which are all the claims pending in the application.

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Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A chimeric monoclonal antibody having variable region of rodent origin and a constant region of human origin which binds to a peptide represented by the amino acid sequence SEQ ID NO:1 in the CD4-binding region of the gp120 of HIV -1 and inhibits in vitro infection of T cells by HTLV-III_B.

The references relied upon by the examiner are:

Neuberger et al. (Neuberger)	WO 86/01533	Mar. 13, 1986
Gilbert et al. (Gilbert)	WO 87/07616	Dec. 17, 1987

Morrison, "Transfectomas Provide Novel Chimeric Antibodies," Science, Vol. 229, pp. 1202-1207 (1985)

Zolla-Pazner et al. (Zolla-Pazner), "Potential use of serotherapy in the prevention and treatment of infection with the human immunodeficiency virus," J. Virological Methods, Vol. 17, pp. 45-53 (1987)

Lasky et al. (Lasky), "Delineation of a region of the human immunodeficiency virus type 1 gp120 glycoprotein critical for interaction with the CD4 receptor," Cell, Vol. 50, pp. 975-985 (1987)

Sun et al. (Sun), "Generation and characterization of monoclonal antibodies to the putative CD4-binding domain of human immunodeficiency virus type 1 gp 120," J. Virology, Vol. 63, pp. 3579-3585 (1989)¹

¹ According to the examiner (Answer, page 5), "[t]he publication date of the Sun reference is subsequent to the effective filing date of the instant application. However, the data presented in Figure 6 on page 3583, are taken from the 1988 publication of Meyers et al. "Human retroviruses and AIDS", the publication date of which is prior to the effective filing date of the instant application." It is unclear to this merits panel why the examiner relied upon Sun instead of Meyers. Nevertheless, we limit our review of Sun to Figure 6 (page 3583).

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GROUND OF REJECTION²

Claims 1, 4, 5 and 7 stand rejected under 35 U.S.C. § 103 as being unpatentable over Lasky in view of Gilbert and Sun and further in view of Neuberger, Morrison and Zolla-Pazner.

We reverse.

DISCUSSION

In reaching our decision in this appeal, we considered appellants' specification and claims, in addition to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer³ for the examiner's reasoning in support of the rejection. We further reference appellants' Brief⁴ for appellants' arguments in favor of patentability.

² Rejections not referred to in Answer are assumed to have been withdrawn. Paperless Accounting, Inc. v. Bay Area Rapid Transit Sys., 804 F.2d 659, 663, 231 USPQ 649, 651-652 (Fed. Cir. 1986), cert. denied, 480 U.S. 933 (1987). In addition, we note the examiner withdrew her Final Rejection (Paper No. 8, mailed May 19, 1994) of claims 1, 4, 5 and 7 under 35 U.S.C. § 112, first paragraph and 101 in the July 7, 1994 Advisory Action (Paper No. 11). In addition, the examiner withdrew her rejection of claims 5 and 7 under 35 U.S.C. § 112, first paragraph in the July 28, 1994 Advisory Action (Paper No. 13). Finally, the examiner withdrew her rejection of claims 1, 4, 5 and 7 under 35 U.S.C. § 103 over Sun, Morrison, Neuberger and Zolla-Pazner in the August 24, 1994 Advisory Action (Paper No. 15).

³ Paper No. 18, mailed January 24, 1995.

⁴ Paper No. 17, received September 28, 1994.

THE REJECTION UNDER 35 U.S.C. § 103:

On this record, the examiner provides two references, Lasky and Gilbert, which teach antibodies specific for epitopes located within the CD4 binding region of HIV-1 gp120. According to the examiner (Answer, page 4) Lasky's Figure 6 (Lasky, page 979) illustrates that the amino acid sequence of the epitope is variable among different HIV-1 isolates. Lasky's Figure 6 also illustrates that 1 sequence (HXB2) of the 12 sequences listed comprises the amino acid sequence of appellants' SEQ ID NO:1. The examiner also finds that Gilbert teach (Answer, bridging sentence, pages 4-5) antiserum raised against a peptide having a sequence that "differs from Seq ID No. 1 of claim 7 by a single residue ([Gilbert's] Peptide 5 has glutamic acid (E) at position 7 ... whereas Seq. ID No: 1 has lysine (K) at this position)."

The examiner relies upon Sun's Figure 6 (Answer, page 5) to establish "that the sequences of the gp120 glycoproteins of various HIV-1 isolates were known in the art at the time the instant invention was made. Figure 6 shows sequences corresponding to the regions containing the CD4 binding sites of fifteen different strains of HIV-1. One of the [15] HIV-1 isolates, designated HXB2, is shown to have a sequence which is identical to that recited in claim 7." The examiner therefore concludes (Answer, bridging sentence, pages 5-6) that Sun "establishes that an HIV-1 isolate having in its CD4 binding domain a

sequence identical to that recognized by the claimed antibodies, was known in the art at the time the claimed invention was made.”

The claimed invention, however, requires the chimeric monoclonal antibody to not only bind “to a peptide represented by the amino acid sequence SEQ ID NO:1 in the CD4-binding region of the gp120 of HIV -1,” but also inhibit “in vitro infection of T cells by HTLV-III_B.” According to the examiner (Answer, page 4) “[t]he 5C2E5 and 7F11 monoclonal antibodies taught by Lasky differ from the claimed antibodies in that they have not been shown to inhibit infectivity of HIV -1 isolates in vitro.” Appellants confirm this arguing (Brief, page 4) that Lasky suggest that their “antibody does not inhibit HIV -1 infection in vitro,” and that when appellants tested Lasky’s antibody they “determined that it does not inhibit HIV -1 infection in vitro.”⁵ With regard to Gilbert, the examiner finds that while Gilbert teaches that antiserum raised against Peptide 5 neutralizes the HIV virus by preventing HIV infection and subsequent lysis of cells, Gilbert does not teach monoclonal antibodies specific for Peptide 5.

Nevertheless, the examiner argues (Answer, bridging paragraph, pages 6-7) that “[i]t would have been obvious to characterize the ability of hybridomas obtained for the production of monoclonal antibodies capable of inhibiting in vitro HIV-1 infectivity using known methods such as those taught by Gilbert.” The examiner reasons (Answer, page 7) that:

⁵ See also Davis Declaration, executed February 7, 1994 at para. 6.

One of ordinary skill in the art would have reasonably expected to obtain cell lines producing antibodies capable of neutralizing HIV -1 infectivity *in vitro* in view of the teaching of Gilbert that polyclonal antibodies elicited against a peptide having a sequence which is nearly identical to that of Seq ID No:1 of the present application, had the ability to inhibit HIV -1 infection *in vitro* and in view of the art-recognized importance of the CD4 binding region of gp120 in virus attachment to CD4 on T cells during the infection process, as evidenced by the teaching of Lasky that antibodies specific for the CD4 binding region of HIV gp120 block viral attachment to CD4 and that anti-CD4 antibodies had been shown to inhibit CD4-gp-120 interaction and inhibit virus infectivity (page 975).

Appellants argue (Brief, bridging paragraph, pages 4-5) that Lasky state that:

“[T]he virus may have evolved mechanisms whereby only low titers of antibodies are directed against CD4 interaction sites, so that the virus may effectively escapes immunosurveillance.” To support this, they [Lasky] note that “in the case of picornaviruses, the receptor-binding site(s) may be buried in a cleft within the viral attachment protein that is unavailable for antibody binding or generation. They [Lasky] also note that the HIV -1 virus may be able to escape neutralization by small mutations in the CD4-binding region. All these statements indicate that neutralizing monoclonal antibodies against the CD4-binding region, as claimed, may be largely ineffective in therapy” [footnote omitted].

To establish a prima facie case of obviousness, there must be both some suggestion or motivation to modify the references or combine reference teachings and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Appellants’ arguments, based on the teaching of Lasky, that “the receptor-binding site(s) may be buried in a cleft within the viral attachment protein that is unavailable for antibody binding or generation,” and the fact that appellants’ found that Lasky’s monoclonal antibody does not inhibit

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HIV-1 infection in vitro, suggest that a person of ordinary skill in the art would not have a reasonable expectation that a single monoclonal antibody would be capable of both binding and inhibiting in vitro infection of T cells by HTLV-III_B. On these facts, Gilbert's teaching that polyclonal antisera to peptide 5 binds an epitope in the CD4 binding region of HIV and neutralizes HIV infection is insufficient to provide one of ordinary skill in the art with a reasonable expectation of successfully obtaining a monoclonal antibody as claimed. In the absence of a reasonable expectation of success, one is left with only an "obvious to try" situation which is not the standard of obviousness under 35 U.S.C. § 103. See In re O'Farrell, 858 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988).

The examiner's reliance on Morrison, Neuberger and Zolla-Pazner fails to make up the deficiency in the combination of Lasky, Gilbert and Sun. On these circumstances, we are constrained to reach the conclusion that the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness as to the claimed cell line.

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Accordingly, we reverse the examiner's rejection of claims 1, 4, 5 and 7 under 35 U.S.C. § 103 over Lasky, Gilbert, Sun, Morrison, Neuberger and Zolla-Pazner.

REVERSED

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SHERMAN D. WINTERS)
Administrative Patent Judge)
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) BOARD OF PATENT
TONI R. SCHEINER)
Administrative Patent Judge) APPEALS AND
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) INTERFERENCES
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