

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 51

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte RUEY S. LIOU, EDWARD M. ROSEN, CECILY ROU-YUN SUN,
BILL NAI-CHAU, SEK C. FUNG, TSE-WEN CHANG
and NANCY T. CHANG

Appeal No. 1997-3274
Application No. 08/015,248

ON BRIEF

Before WINTERS, WILLIAM F. SMITH and SCHEINER, Administrative Patent Judges.
SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 12, 27 and 30, the only claims remaining in the application. The claims read as follows:

12. A chimeric immunoglobulin comprising an antigen binding region derived from the murine immunoglobulin BAT123 or an immunoglobulin which specifically binds to the same epitope as BAT123 and a human constant region.

27. A chimeric monoclonal immunoglobulin having a variable region of rodent origin and a constant region of human origin which binds to an epitope within a peptide including amino acid residue numbers 308 to 322 of gp120 of HIV-1_B, as designated by the numbering system set forth in Human Retroviruses and AIDS 1990, Loa Alamos National Laboratory (Eds. Myers, G. et al.).

30. A chimeric monoclonal immunoglobulin having a variable region of rodent origin and a constant region of human origin which binds to the amino acid sequence RIQRGPGRAFVTIGK.

The references relied on by the examiner are:

Montagnier et al. (Montagnier) WO 86/02383 Apr. 24, 1986

Kennedy et al. (Kennedy) WO 87/02775 May 7, 1987

Roberts-Gurdoff et al. (Roberts-Gurdoff), "HTLV-III-Neutralizing Antibodies in Patients with AIDS and AIDS-Related Complex," Nature, Vol. 316, pp. 72-74 (Jul. 4, 1985)

Morrison, "Transfectomas Provide Novel Chimeric Antibodies," Science, Vol. 229, pp. 1202-1207 (Sep. 20, 1985)

THE REJECTION

This case has been returned to the jurisdiction of the board following a remand to the examiner; the sole issue remaining before us is whether the examiner was correct in maintaining the rejection of claims 12, 27 and 30 under 35 U.S.C. § 103 as unpatentable over Montagnier, Kennedy, Roberts-Gurdoff and Morrison.

DISCUSSION

Claim 12 is directed to a chimeric antibody with a human constant region and a murine antigen binding region - the antigen binding region is either derived from the murine antibody BAT123, or binds the same epitope bound by BAT123. Claims 27 and 30 are directed to chimeric antibodies having human constant regions and rodent variable regions specific for an epitope within a peptide including amino acid residue numbers 308 to 322 of gp120 of HIV-1_B (as designated by the numbering system set forth in Human Retroviruses and AIDS 1990, Los Alamos National Laboratory), i.e., chimeric antibodies specific for an epitope within the sequence RIQRGPGRAFVTIGK - the same sequence used to raise BAT123.

Montagnier discloses at least thirty specific amino acid sequences deduced from the nucleotide sequence of the lymphadenopathy associated virus - one of which has the sequence LNQSVEINCTRPNNNTRKSIRIQRGPGR. According to Montagnier,

“[t]he different peptides” based on the deduced sequences can be used “for the production of antibodies, preferably monoclonal antibodies specific [for] the different peptides respectively.” Pages 29 and 46.

Kennedy describes six synthetic peptides “selected on the basis of . . . predicted immunogenicity,” which were used to raise polyclonal antibodies in rabbits. Page 7. One of Kennedy’s peptides has the sequence TRPNNTRKSIRIQRGPG.

According to the examiner, “Morrison teaches conventional methods for the production of chimeric antibodies,” and “one of ordinary skill in the art would have found it obvious to manipulate the antibodies . . . to prepare chimeric antibodies using [Morrison’s] generally applicable methods . . . for a variety of reasons[; o]ne of which is described [by] Roberts-Guroff [who teaches] the potential therapeutic utility of anti-HIV antibodies for the treatment of AIDS,” and a second, “described [by Morrison,] which would be for obtaining varying effector functions that may yield in vitro applicability.” Answer, pages 10 and 11. In addition, the examiner asserts that the prior art peptides “were known to be immunogenic and to elicit antibodies capable of neutralizing HIV infectivity in vitro.”

We find the examiner’s rejection to be without merit for several reasons.

The examiner concedes that “[n]one of the references teach[es] chimeric immunoglobulins specific for the peptides described above.” Answer, page 9. We would also add that none of the references appears to teach any sort of antibody specific for the same epitope as BAT123, a specificity required by claim 12. BAT123 was raised against a synthetic peptide immunogen with the amino acid sequence RIQRGPGRAFVTIGK, and the present specification suggests that BAT123 reacts “with

an epitope borne by either all or a part of the middle five amino acids [(i.e., PGRAF)] or a combination of these amino acids with some of the flanking amino acids.”¹ Page 69. The closest peptide immunogen described by Montagnier has the amino acid sequence LNQSVEINCTRPNNNTRKSIRIQRGPGR, which overlaps with the fifteen amino acid BAT 123 peptide over a stretch of eight amino acids - only three of which (underlined) correspond to middle five amino acids (the putative BAT123 epitope). Similarly, Kennedy raises polyclonal antibodies against six peptides, one of which has the sequence TRPNNNTRKSIRIQRGPG - in this case, the peptide overlaps with the BAT123 peptide for a stretch of seven amino acids, only two of which (underlined) correspond to the putative BAT123 epitope. In our view, the examiner has not established that either Montagnier or Kennedy discloses peptide immunogens which would elicit antibodies specific for the same epitope as BAT123.

Claims 27 and 30 are somewhat broader than claim 12, in that they merely require chimeric antibodies that bind an epitope somewhere in the amino acid sequence used to raise the BAT123 antibody, i.e., somewhere in the amino acid

¹ According to the specification, three monoclonal antibodies, BAT123, BAT267 and BAT085, “showed very clear and specific reactivities with particular peptides in [a] Western blot assay . . . The 15 amino acid long peptides reactive with BAT267 and BAT123 overlap by 5 amino acids [at the carboxy-terminus of the BAT123 peptide, but], the antibodies react with just one of them and do not react with the other to any measurable extent. The antibodies do not react with peptides overlapping at the other ends either . . .” Specification, paragraph bridging pages 68 and 69.

sequence RIQRGPGRAFVTIGK. Nevertheless, it is not enough to argue, as the examiner has, that “there is nothing of record to suggest the criticality of the differences between the referenced peptides and those recited in [the] claims.” Answer, page 11.

The claims are directed to antibodies, not peptide immunogens. If the examiner is alleging that antibodies raised against Montagnier’s peptides or Kennedy’s peptides would inherently bind the peptide used to raise BAT123, then the examiner has the initial burden of coming forward with evidence that supports that position. The burden of proof shifts to appellants only if the examiner’s assertion of inherency has a reasonable basis in fact - a conclusory statement on the part of the examiner is not enough to shift the burden. See In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). If, on the other hand, the examiner is alleging that the specificity of the antibodies raised against the various peptides would not differ in any “critical” way, we would remind the examiner that “the examiner bears the initial burden of presenting a prima facie case of obviousness” and “[o]nly if that burden is met, does the burden of coming forward with evidence or argument shift to [appellants].” In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). Thus, the criticality of a limitation is immaterial if there is nothing in the prior art to suggest the limitation in the first place.

The specificity of the prior art antibodies aside, we also disagree with the examiner’s conclusion that it would have been obvious to convert the prior art antibodies to chimeric antibodies with human constant regions. As discussed above, the examiner proposes two separate theories for combining the references. First, that it would have been obvious to make chimeric antibodies for in vivo applications because Roberts-Guroff suggests that neutralizing antibodies may be protective, while “peptides corresponding to the amino acid sequence in the region of residues 298-322 were

known . . . to elicit antibodies capable of neutralizing HIV infectivity in vitro.” Answer, page 11. Second, that it would have been obvious to make chimeric antibodies for in vitro applications because Morrison suggests that varying effector functions may yield in vitro applicability. Id., pages 10 and 11.

Having reviewed the Robert-Guroff reference, and the analysis of the reference set forth in paragraphs 2-4 of Dr. Davis’ declaration of November 5, 1993, we would not go so far as to conclude, as appellants did in their brief, that the reference “suggest[s], on balance, that neutralizing anti-HIV-1 monoclonal antibodies will not be effective for therapy.” Brief, page 12 (emphasis added). On the other hand, we do think it is reasonable to conclude, as Dr. Davis did in the declaration, that Robert-Guroff stops short of suggesting “that neutralizing anti-HIV-1 antibodies can be administered to combat HIV-1.” Declaration, page 2. Moreover, we see no basis for the examiner’s statement that peptides representing the amino acid sequence in the region of residues 298-322 were known to elicit neutralizing antibodies. We see no evidence in Kennedy that peptide 2 (the closest to the BAT123 peptide) actually elicited neutralizing antibodies - Kennedy’s disclosure in this regard appears to be merely prophetic. On this record, we agree with appellants that “none of the references of record suggest that anti-HIV-1 antibodies should be used in vivo,” and “[t]here is, therefore, no suggestion to make the claimed chimeric antibodies” for in vivo applications. Brief, page 14.

Similarly, having reviewed the Morrison reference, in light of Dr. Davis’ analysis of the reference in paragraphs 6 through 12 of the declaration executed November 5, 1993, we agree with appellants that there is no suggestion in Morrison that “chimeric antibodies, having a human constant region, should be used in in vitro assays.” Brief, page 16.

“In proceedings before the Patent and Trademark Office, the examiner bears the

burden of establishing a prima facie case of obviousness based upon the prior art.

‘[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.’” In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citations omitted). “To imbue one of ordinary skill in the art with knowledge of the invention . . . , when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.” W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1552, 220 USPQ 303, 312-313 (Fed. Cir. 1983).

The references cited by the examiner do not teach or suggest all of the limitations of the instant claims and therefore do not support a prima facie case of obviousness. The rejection of the claims under 35 U.S.C. § 103 is reversed.

REVERSED

Sherman D. Winters
Administrative Patent Judge

William F. Smith
Administrative Patent Judge

)
)
)
)
) BOARD OF PATENT
)
) APPEALS AND
) INTERFERENCES
)
)

Appeal No. 1997-3274
Application No. 08/015,248

Page 8

Toni R. Scheiner)
Administrative Patent Judge)

Eric P. Mirabel
Tanox Biosystems, Inc.
10301 Stella Link #110
Houston, TX 77025-5497