

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte STELLA QUAN,
PABLO VALENZUELA and ALAN POLITO

Appeal No. 2003-1679
Application No. 08/993,010

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 1-3, 6-10, 13-17, 20-22 and 24. Claims 25-44 were withdrawn from consideration as a result of a restriction requirement.¹

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

1. A method of detecting Helicobacter pylori antibodies associated with infection in a human subject comprising:
 - (a) reacting a biological sample from the subject with one or more H. pylori type-common antigens provided in an H. pylori lysate and with one or more purified type-specific H. pylori Type I

¹ We note there is some degree of confusion regarding the status of claim 24. The examiner's statement of the status of the claims lists claim 24 as both involved in this appeal, and as withdrawn from consideration. Answer, page 2. Similarly, appellants' Brief (page 2), identifies claim 24 as withdrawn. However, since the examiner has rejected claim 24 under 35 U.S.C. § 103, we have considered claim 24 in our deliberations.

- antigens, wherein the type-specific antigens are H. pylori vacuolating cytotoxin (VacA) and cytotoxin associated antigen (CagA), under conditions which allow H. pylori antibodies, when present in the biological sample, to specifically bind with said type-common antigens or said type-specific antigen(s),
- (b) removing unbound antibodies;
 - (c) providing one or more moieties comprising a detectably labeled anti-human immunoglobulin antibody which bind to said bound antibodies;
 - (d) detecting the presence or absence of said one or more moieties;
 - (e) correlating the presence of antibodies that specifically bind to the type-specific antigens to infection with Type I H. pylori; and
 - (f) correlating the absence of antibodies that specifically bind to the type-specific antigens and the presence of antibodies that specifically bind to the type-common antigens to infection with Type II H. pylori.

The references relied upon by the examiner are:

Crabtree et al. (Crabtree), "Mucosal Humoral Immune Response to Helicobacter pylori in Patients with Duodenitis," Digestive Diseases and Sciences, Vol. 36, No. 9, pp. 1266-1273 (1991)

Telford et al. (Telford), "Unraveling the pathogenic role of Helicobacter pylori in peptic ulcer: potential new therapies and vaccines," TIBTEC, Vol. 12, No. 10, pp. 420-436 (1994)

Figura, "Progress in defining the inflammatory cascade," European Journal of Gastroenterology & Hepatology, Vol. 7, No. 4, pp. 296-302 (1995)

Xiang et al. (Xiang), "Analysis of Expression of CagA and VacA Virulence Factors in 43 Strains of Helicobacter pylori Reveals that Clinical Isolates Can Be Divided into Two Major Types and that CagA Is Not Necessary for Expression of the Vacuolating Cytotoxin," Infection and Immunity, Vol. 63, No. 1, pp. 94-98 (1995)

GROUNDINGS OF REJECTION

Claims 1-3, 6-10 and 13-17² stand rejected under 35 U.S.C. § 103 as being unpatentable over Figura in view of Xiang and Crabtree.

² We note the following typographical error. In the statement of this rejection, the examiner included claims 11 and 18. Since claims 11 and 18 are cancelled, we have not included these claims in our deliberation.

Claims 20-22 and 24 stand rejected under 35 U.S.C. § 103 as being unpatentable over Figura in view of Xiang and Crabtree and further in view of Telford.

We reverse.

DISCUSSION

Figura in view of Xiang and Crabtree:

The examiner finds (Answer, page 4), “Figura define *Helicobacter pylori* strains by dividing them into two phenotypically distinct groups: Type I strains express VacA and CagA; and Type II do not express VacA and CagA proteins....” The examiner also finds (id.), Figura teach “[a] method of detecting antibodies associated with *Helicobacter pylori* infection in humans....” According to the examiner (Answer, page 5), Figura’s method of detecting antibodies associated with Helicobacter infection comprises:

(a) reacting a biological sample from a subject with one or more H.[]*pylori* type common antigens and one or more Type-I specific antigens provided in an H.[]*pylori* whole cell preparation (lysate) from a Type-I specific strain (see page 299, figure 5, narrative, line 4). The common type antigens were shown to be urease subunits A and B and H.[]*pylori* heat shock protein, and the Type-I specific antigens shown were both VacA and CagA antigens,

(b) removing unbound antibodies in light of the method being incorporated by reference to Xiang who teaches the removal of unbound antibodies (Xiang, page 95, col. 2, last paragraph, lines) (see Figura reference, page 298, col. 2, paragraph 6, reference [1] is Xiang et al, 1995),

(c) providing a moiety to detect antibodies that specifically bound to common and Type-I specific antigens were visualized (see Figure 5 immunoreactive bands), and

(d) detecting the presence or absence detectably labeled anti-human immunoglobulin antibody, thereby detecting the presence or absence of H.[]*pylori* antibodies associated with

infection in the subject.

The examiner relies on Xiang to teach a method using Western blot to distinguish between Type I and Type II H. pylori clinical isolates based upon VacA and CagA expression. Answer, page 7. The examiner relies on Crabtree (Answer, page 7), to teach “the use of a detectably labeled anti-human immunoglobulin antibodies in an analogous art for the purpose of detecting human antibodies associated with Helicobacter pylori infection ... in subject serum samples.”

According to the examiner (id.), Figure 5, lanes 3-6 of Figura demonstrate that Figura distinguished Type I and Type II antibodies present in human serum samples “through specific binding of common Type II and Type I specific antigens,” wherein lane 6 illustrates “[a]ntibodies to Type II antigens were detected, no binding to VacA or CagA,” and lanes 3-5 illustrate “antibodies to one or more Type I specific antigens were detected.”

Based on this evidence, the examiner finds (Answer, bridging sentence, pages 7-8), “it would have been prima facie obvious to a person of ordinary skill in the art [sic] the time the invention was made ... to utilize detectably labeled anti-human immunoglobulin to detect the presence or absence of human antibodies that specifically bound to Helicobacter common and Type-I specific antigens...”

Appellants, however, point out (Brief, page 11) that Figura “fails to establish a definitive correlation between expression of VacA and CagA antigens and infectivity.” In addition, appellants emphasize (id., emphasis removed), Figura admits “that CagA and VacA expression does not necessarily correlate

with infectivity. (Figura, page 298, right column; Figure 5 and accompanying legend).”

Figura characterizes H. pylori Type I strains as expressing VacA and CagA, and Type II strains as being VacA- and CagA-negative. See Figura, Abstract. Consistent with appellants’ analysis (Brief, page 11), Figura teaches (page 298, second column, last paragraph, endnotes omitted), Western blots

are not quantitative and sometimes difficult to interpret. In Fig. 5, for example, disparate immune responses to CagA and VacA can be observed (lanes 3 to 5). These proteins are expressed together in more than 70% of H. pylori isolates. Surprisingly, out of the hundreds of Western blots we have performed, VacA immune recognition was observed in only about 15% of cases in which serum samples reacted with CagA, and in about 5% of cases which were seronegative for CagA. Although the results of Xiang et al. explain the existence of strains expressing only VacA (in about 10% of isolates), the examples shown in Fig. 5 indicate that more studies are needed to clarify the situation in vivo.

We remind the examiner, that in order 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). On this record, while Figura refers to Xiang to “explain the existence of strains expressing only VacA,” Figura expressly states that “more studies are needed to clarify the situation in vivo.” In this regard, notwithstanding the examiner’s position to the contrary (Answer, page 16, paragraph 15), appellants’ claimed invention is directed to a method of detecting Helicobacter pylori antibodies associated with infection in a human subject comprising, inter alia, correlating the presence of antibodies that bind to specific antibodies to either

infection with Type I or Type II H. pylori. As appellants' point out (Brief, page 11), Figura makes no such correlation, but instead, expressly states that more studies are necessary. Furthermore, while both Figura and the examiner direct our attention to Xiang, Xiang classifies some CagA- and VacA-negative H. pylori strains as Type I, and others as Type II. See Xiang, page 95, Table 1, strains 32, 33, and 36-43. Accordingly, we agree with appellants' (Brief, page 13), Xiang does not provide a clear "correlation between anti-CagA and anti-VacA antibodies and [T]ype I infection."

In this regard, we note the examiner's reference to Xiang, page 97, second column, third paragraph. Answer, page 19. This portion of Xiang notes only that "Type II bacteria do not have the gene coding for CagA and do not produce CagA..." there is no discussion or recognition that the VacA antigen is also associated with Type I strains, as is required by appellants' claimed invention. With regard to VacA, Xiang discusses the possibility of "intermediate phenotypes." See Xiang, page 97, column 2, paragraphs 5 and 6; Answer, page 19. However, Xiang expressly states (first sentence, bridging paragraph, pages 97-98), "[f]rom these observations, we conclude that an understanding of the linked expression of CagA and VacA must await characterization of the genetic differences between [T]ype I and [T]ype II bacteria..." Based on this evidence, it is our opinion that Xiang failed to recognize that CagA and VacA were associated with Type I H. pylori. We remind the examiner, in determining whether the claimed invention is obvious, a prior art reference must be read as a whole and consideration must be given where the reference teaches away from the claimed

invention. Akzo N.V., Aramide Maatschappij v.o.f. v. United States Int'l Trade Comm'n, 808 F.2d 1471, 1481, 1 USPQ2d 1241, 1246 (Fed. Cir. 1986).

We note the examiner's assertion (Answer, page 15), "[i]t is the position of the examiner that Figura in view of Xiang clearly provides a reasonable expectation of success in detecting the presence of humoral Type I and Type II antibodies (see Figure 5) indicative of H. pylori Type I or Type II strains infecting the patient." However, as discussed above, on this record, neither Figura nor Xiang provide a correlation of the presence or absence of specific antibodies to infection with Type I or Type II H. pylori. While the examiner has asserted that a correlation exists, the evidence of record does not support this assertion. We remind the examiner that "to imbue one of ordinary skill in the art with knowledge of the invention in suit, 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 & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

Crabtree, relied upon by the examiner (Answer, page 7) to teach "the use of a detectably labeled anti-human immunoglobulin antibodies..." fails to make up for the deficiencies in the combination of Figura and Xiang. Accordingly, we reverse the rejection of claims 1-3, 6-10 and 13-17 under 35 U.S.C. § 103 as being unpatentable over Figura in view of Xiang and Crabtree.

Figura in view of Xiang and Crabtree and further in view of Telford:

Claim 20 is drawn to a method of monitoring a human subject undergoing therapy for Helicobacter pylori infection comprising, inter alia, the method of detecting Helicobacter pylori antibodies as set forth in claim 1.

The combination of Figura in view of Xiang and Crabtree was discussed above. While not clearly articulated by the examiner (see Answer, pages 9 and 28-29), it appears that the examiner relies on Telford to teach (bridging paragraph, pages 421-422), “a simple scheme, in which all H. pylori strains could be partitioned into two groups, which either express (Type I) or do not express (Type II) the cytotoxin [VagA] and the CagA proteins.”

We note, however, that Telford published before either of the Figura or Xiang references. As discussed above, with regard to Figura and Xiang, the later published evidence on this record teaches away from the “simple scheme” discussed by Telford. To establish a prima facie case of obviousness, the examiner must show “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 Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). There is no suggestion to combine, however, if a reference teaches away from its combination with another source. See id. at 1075, 5 USPQ2d at 1599. “A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant ... [or] if it suggests that the line of development flowing from the reference's disclosure is

unlikely to be productive of the result sought by the applicant.” In re Gurley, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). In our opinion, for the reasons discussed above, both Figura and Xiang would have led a person of ordinary skill in the art at the time the invention was made away from the simple scheme discussed by Telford, and accordingly, away from appellants’ claimed invention.

Accordingly, we reverse the rejection of claims 20-22 and 24 under 35 U.S.C. § 103 as being unpatentable over Figura in view of Xiang and Crabtree and further in view of Telford.

Having determined that the examiner has not established a prima facie case of obviousness, we find it unnecessary to discuss the del Giudice Declaration, relied on by appellants (Brief, pages 20-23) to rebut any such prima facie case.

REVERSED

Sherman D. Winters)	
Administrative Patent Judge)	
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Toni R. Scheiner)	
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