UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte
LING CHEN, JOHN W. SHIVER, ANDREW J. BETT,
DANILO R. CASIMIRO, MICHAEL J. CAULFIELD,
MICHAEL A. CHASTAIN, and EMILIO A. EMINI

Appeal 2007-4519
Application 10/461,030
Technology Center 1600

Decided: July 14, 2008

Before TONI R. SCHEINER, LORA M. GREEN, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 21 and 22. We have jurisdiction under 35 U.S.C. § 6(b). Claim 21 is representative of the claims on appeal, and reads as follows:

21. A method for inducing a cellular immune response against an HIV protein in an individual which comprises administering to the individual a replication-defective adenovirus vector which comprises a gene expression cassette; said replication-defective adenovirus vector lacking a functional E1 gene; and said gene expression cassette comprising nucleic acid encoding an HIV gag protein which is codon optimized for expression in a human host.

We affirm.

DISCUSSION

Claims 21 and 22 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Prevec,[1] Toloza,[2] and André.[3]

Prevac is cited for teaching a recombinant adenovirus vector containing a deletion in the E3 region that expresses the human immunodeficiency virus (HIV) *gag* gene (Ans. 4). According to the Examiner, the vector is replication defective (*id.*). The Examiner notes further that Prevac teaches that the vectors "'were able to induce an immune response in mice and rhesus macaque monkeys.'" (Ans. 4 (quoting Prevac, p. 573, right col).) The Examiner notes that Prevac "does not disclose a

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[1] Prevac, "Immune Response to HIV-1 gag Antigens Induced by Recombinant Adenovirus Vectors in Mice and Rhesus Macaque Monkeys," *Journal of Acquired Immune Deficiency Syndromes*, Vol. 4, pp. 568-576 (1991).

[2] Toloza, "Transduction of Murine and Human Tumors Using Recombinant Adenovirus Vectors," *Annals of Surgical Oncology*, Vol. 4, pp. 70-79 (1997).

[3] André, "Increased Immune Response Elicited by DNA Vaccination with a Synthetic gp120 Sequence with Optimized Codon Usage," *J. Virol.*, Vol. 72, pp. 1497-1503 (1998).

'replication-defective' adenovirus carrying a mutated E1 coding region or a *gag* gene that has been optimized for human expression." (Ans. 4.)

Toloza is cited for teaching "the preparation of replication-deficient adenoviruses carrying an expression cassette that lack a functional E1 region." (Ans. 4 (emphasis removed).) The Examiner further cites Toloza for teaching that the "constructs were capable of transducing human cells with high efficiency and resulted in persistent gene expression in the target of interest." (*Id.*)

André is cited for teaching that immunization with a codon-optimized HIV *env* gene resulted in increased antibody titers and cytotoxic T-lymphocyte activity (Ans. 4).

The Examiner concludes

> it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the parental Ad5Δ[E]3 vector of Prevec *et al.* (1991) with the Ad5ΔE1 vector disclosed by Toloza *et. al.* (1997), since Toloza and colleagues teach that this construct can transduce human cells with high efficiency and leads to persistent transgene expression. Moreover, it would have also been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to codon optimize the *gag* gene disclosed by Prevec *et al.* (1991) for human expression since Andre et al. (1998) teach that codon optimized HIV structural genes induce stronger humoral and cell-mediated immune responses than their non-optimized counterparts. Thus, both a reasonable expectation of success and the motivation to do so, can be found in the prior art.

(Ans. 5.)

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or

argument shift to the applicant." *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citations omitted). In order to determine whether a prima facie case of obviousness has been established, we consider the factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966): (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the relevant art; and (4) objective evidence of nonobviousness, if present.

Appellants argue that Prevac discloses replicating adenoviral vectors, and that the use of replication-defective vectors is not taught or suggested by that reference (App. Br. 14). Appellants cite Hitt, [4] Bout,[5] Ho,[6] Fields,[7] and Rich,[8] to support their position that Prevac in fact discloses a replicating adenoviral vector (Reply Br. 6-7). Appellants argue further, again citing Hitt, that "one would expect a replicating adenovirus to have a dramatically higher copy number of virus and a consequently higher level of recombinant gene expression." (App. Br. 14.)

Toloza, Appellants argue, is drawn to cancer vaccines, and the use of replication-defective adenovirus vectors in cancer is not predictive of their use in an HIV vaccine (*id.*). Moreover, Appellants assert, the vectors of Toloza are used to transduce tumor cells to express a cytokine, and it is the

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[4] Hitt, "Human Adenovirus Vectors for Gene Transfer into Mammalian Cells," *Adv. Pharmacol.*, Vol. 40, pp. 137-206 (1997).
[5] Bout, EP 0707071 A1, published April 17, 1996.
[6] Ho, U.S. Patent No. 6,040,171, issued March 21, 2000.
[7] Fields, Virology, Second Edition (B.N. Fields et al., eds), Raven Press, Ltd. Ch. 60 (1990).
[8] Rich, "Development and Analysis of Recombinant Adenoviruses for Gene Therapy of Cystic Fibrosis," *Hum. Gen. Ther.*, Vol. 4, pp. 461-476 (1993).

resultant population of tumor cells that is to be used as the cancer vaccine (*id.* at 15).

The Examiner does not respond to Appellants' arguments that Prevac in fact discloses a replicating adenovirus (*see, eg.*, Ans. 6; *see also* Office Action of April 16, 2007, p. 1 (Noting Reply Brief)). Moreover, the Examiner does not point to, and we cannot find, anything in the Prevac reference to support the Examiner's position that Prevac teaches a replication-defective adenovirus vector. And the references cited by Appellants do establish that adenovirus vectors that have the E3 region deleted are not necessarily replication defective. For example, as noted by Hitt, "[v]iruses with only E3 deleted . . . are replication proficient." (Hitt, p. 142.) Thus, the evidence of record supports Appellants' position that Prevac in fact discloses a replicating adenovirus.

The Examiner does argue that Toloza provides "the same replication-defective ΔE1 adenoviral vectors as currently claimed." (Ans. 6.) However, an invention "composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). "Often, it will be necessary . . . to look to interrelated teachings of multiple [references] . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed[.]" *Id.* at 1740-41. "[T]his analysis should be made explicit" (*id.* at 1741), and it "can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" (*id.*).

Here, the Examiner has not provided sufficient reason as to why the ordinary artisan would have used the replication defective adenovirus vector of Toloza, which is drawn to the use of the vector to engineer tumor cells that express a cytokine for use as a tumor vaccine (Toloza, p. 70), for the replication competent adenovirus vector for use as an HIV vaccine as taught by Prevac. For instance, the Examiner states that "antigens expressed from these vectors [of Toloza] were clearly capable of inducing a strong immune response" (Ans. 6), but provides no evidence to support this position when such vectors were used to produce a cytokine, not an immune response against a viral HIV protein. Simply put, the Examiner has not made a prima facie case based on the prior art relied upon in the rejection as to why the ordinary artisan would move from a replication competent virus to a replication incompetent adenovirus. We are thus compelled to reverse the rejection.

Claims 21 and 22 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-20 of U.S. Patent No. 6,787,351 B2 (Chen, issued September 7, 2004) (Ans. 5).

Appellants do not argue the merits of the rejection, but only state that "upon official notice that subject matter is deemed allowable, Appellants [will] submit an appropriate terminal disclaimer to remove the double patenting rejection." (App. Br. 16.) We therefore summarily affirm this rejection.

CONCLUSION

In summary, we reverse the rejection of claims 21 and 22 under 35 U.S.C. § 103(a) as being obvious over the combination of Prevec, Toloza, and André, but affirm the rejection of claims 21 and 22 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-20 of U.S. Patent No. 6,787,351 B2.

No time period taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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