

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 25

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte YUJI NOGUCHI, YAO-TSENG CHEN,
and LLOYD J. OLD

Appeal No. 1999-1422
Application No. 08/408,915

ON BRIEF

Before ROBINSON, MILLS, and GRIMES, Administrative Patent Judges.
ROBINSON, 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 1, 2, 5 - 8, 11 - 13, and 15, which are all of the claims pending in this application.

Claims 1, 8, and 11 are illustrative of the claims on appeal and are reproduced below:

1. Composition useful in provoking an immune response comprising an amount of (i) an immunogenic p53 derived protein or peptide, (ii) an adjuvant, an (iii)

Appeal No. 1999-1422
Application No. 08/408,915

interleukin-12 sufficient to provoke an immune response, wherein said interleukin-12 is present in an amount of no more than 1 ng per 100 µg of said immunogenic p53 derived protein or peptide, but is present in an amount sufficient to provoke an immune response.

8. Kit useful in provoking an immune response, comprising a container means and a separate portion of each of

(i) an immunogenic p53 derived protein or peptide,

(ii) an adjuvant, and

(iii) interleukin-12, wherein said interleukin-12 is present in an amount of 1 ng or less per 100 µg of (i).

12. The method of claim 11, wherein said immune response is a T cell response.

The references relied on by the examiner are listed below:

Levine	WO 94/02167	Feb. 3, 1994
Paoletti et al. (Paoletti)	WO 94/16716	Aug. 4, 1994

Livingston, "Construction of cancer vaccines with carbohydrate and protein (peptide) tumor antigens," Curr. Opin. Immunol., Vol. 4, pp. 624-629 (1992)

Brunda et al. (Brunda), "Antitumor and antimetastatic activity of interleukin 12 against murine tumors," J. Exp. Med., Vol 178, pp. 1223-1230 (1993)

Hall, "IL-12 holds promise against cancer, glimmer of AIDS hope," Science, Vol. 263, pp. 1685-1686 (1994)

Nijman et al. (Nijman), "p53, a potential target for tumor-directed T cells," Immunol. Lett., Vol. 40, pp. 171-178 (1994)

Appeal No. 1999-1422
Application No. 08/408,915

Grounds of Rejection

Claims 1, 2, 5 - 8, 11 - 13 and 15 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on a non-enabling disclosure.

Claims 1, 8, 11, 12, and 15 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Levine, Paoletti, and Hall.

Claim 2 stands rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Levine, Paoletti, Hall, and Nijman.

Claims 6, 7, and 13 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Levine, Paoletti, Hall, and Livingston.

We reverse these rejections for the reasons set forth herein.

The claimed invention

The claimed invention is directed to a composition, which is stated to be useful in provoking an immune response, which is comprised of an immunogenic p53 derived protein or peptide, an adjuvant, and interleukin-12 (IL-12), wherein the IL-12 is present in an amount of no more than 1 ng per 100 µg of the immunogenic p53 derived protein or peptide, but is present in an amount sufficient to provoke an immune response. (Claim 1). Claim 8 is directed to a kit, which is said to be useful in provoking an immune response, comprised of a container means, a separate portion of each of an immunogenic p53 derived protein or peptide, an adjuvant, and IL-12 wherein the IL-12 is present in an

Appeal No. 1999-1422
Application No. 08/408,915

amount of 1 ng or less per 100 µg of the immunogenic p53 derived protein. Claim 12 is directed to a method for provoking an immune response in a subject by administering the composition of claim 1 to said subject. The specification, at page 6, states that the immunogen of the invention includes all p53 derived peptides or protein. We read the claims and the specification to indicate the wild-type p53 is not encompassed by that part of the claim which calls for a p53 derived protein or peptide.

Discussion

The rejection under 35 U.S.C. § 112, first paragraph

When an issue of enablement is raised under 35 U.S.C. § 112, first paragraph, the initial burden is on the Patent and Trademark Office to establish reasons why one skilled in the art would not believe the objected statements of utility and/or enablement in the specification. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

In setting forth the basis of the rejection under 35 U.S.C. § 112, first paragraph, the examiner initially acknowledges that the specification “discloses a wild type p53 peptide and a corresponding mutant p53 peptide with a single point mutation at codon 234 of the wild type p53 (pages 8-9).” (Answer, page 4). However the examiner urges that (id.):

[t]he specification does not teach the required features of p53 which provoke an immune response, thus it would require undue experimentation to determine which amino acids to substitute in the wild type p53 (which does not provoke an immune response) in order to obtain mutated p53 proteins which would result in provoking an immune response.

Appeal No. 1999-1422
Application No. 08/408,915

The examiner, further, explains that (Answer, page 9):

the specification does not explain the significance of the choice of codon 234 as the site of mutation, nor does it teach that mutations at any other site on any other wild type p53 would boost an immune response as claimed. Thus, the specification does not provide guidance for determining the required feature(s) of p53 which distinguish between one forms ability to provoke an immune response while another does not, nor does the specification teach how to select these forms of p53.

In rebuttal, appellants urge that the state of the art, as represented by Nijman describes immunogenic peptides and the manner in which they generate immune response as well as assays for determining which peptides generate an immune response as required by the present claim. (Brief, pages 5-6). Thus, appellants urge that "[t]here is no need to carry out an inordinate or undue amount of experimentation to enable the invention as claimed, because immunogenic p53 peptides are known . . . [and] the art, as per Nijman, teaches how to determine whether or not a T cell response is generated. The examiner never comes to grips with these arguments, but continues to focus on the amount of guidance provided by the disclosure in support of the claimed invention. (Answer, page 9). However, the guidance provided by the disclosure of the invention is merely one of the factors which should be considered in determining whether a rejection of lack of enablement should be made. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Here the examiner has not established by substantive evidence or sound scientific reasoning why one skilled in this art could not have practiced the claim

Appeal No. 1999-1422
Application No. 08/408,915

invention through out its scope, given the disclosure provided in support thereof, without undue experimentation.

Thus, on the record before us, we find that the examiner's statements, in support of these rejections, fail to provide a factual basis for the conclusions reached and fail to provide adequate evidence or reasons why one skilled in the art would doubt the statements relating to whether the scope of the claims, as they relate to the p53 derived protein or peptide as called for by the appealed claims is enabled. We, therefore, reverse the rejection under 35 U.S.C. § 112, first paragraph.

The rejections under 35 U.S.C. § 103

Claims 1, 8, 11, 12, and 15 stand rejected under 35 U.S.C. § 103 as being obvious over the combination of Levine, Paoletti and Hall.

The examiner relies on Levine as describing a composition useful in provoking an immune response comprising a p53 derived protein or peptide and an adjuvant and the administration of this combination for treating cancer. (Answer, paragraph bridging pages 5-6). The examiner acknowledges that Levine does not describe a composition containing IL-12 in combination with the p53 derived peptide or protein. (Id.). The examiner relies on Hall as describing IL-12 as having a broad range of antitumor activity

Appeal No. 1999-1422
Application No. 08/408,915

while referencing Brunda¹, cited in Hall, as describing a dose of 0.001 µg (1 ng) to provide an immune response. The examiner relies on Paoletti as describing (Answer, page 6):

an immunogenic composition containing a recombinant virus which includes a DNA sequence which encodes a tumor associated antigen and a cytokine. . . Paoletti et al exemplify p53 as the tumor associated antigen (page 22, line 22) and IL-12 as the cytokine (page 25, line 31; page 26, line 6).

The examiner concludes that (Answer, page 10):

it would have been prima facie obvious to one of ordinary skill in the art to combine p53, adjuvant and IL-12 in combination to provoke an immune response against tumor challenge. In addition, the specification does not teach a patentable distinction between the composition claimed and the composition in a kit form, thus, a kit form of the composition would have also been obvious.

On this record, the examiner does not explicitly explain how one goes from the teachings of the individual references to the conclusion that the present combination of ingredients would have been obvious within the meaning of 35 U.S.C. § 103. To the extent that the examiner would urge that Paoletti provides the suggestion and/or direction to combine an immunogenic protein or peptide derived from p53 with an adjuvant and IL-12,

¹ We would note that the examiner has not included Brunda in the list of references relied on or in the statement of the rejection. However, it would appear from the Answer, that the examiner is relying on Brunda to provide that which Hall does not explicitly provide. Where a reference is relied on to support a rejection, whether or not in a "minor capacity," there would appear to be no excuse for not positively including the reference in the statement of rejection. In re Hoch, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n. 3 (CCPA 1970)

Appeal No. 1999-1422
Application No. 08/408,915

we would note that Paoletti does not describe the combination of substances in this form. While Paoletti may generically include DNA sequences which would encode these or similar proteins, this does not reasonably suggest the use of the individual substances, which may be encoded by the DNA sequences described. In fact, we find nothing in Paoletti which would suggest the likelihood that such a combination would even be useful in the treatments described.

To the extent that the examiner would urge that the combination of two such ingredients as presently called for by the appealed claims would naturally follow from the fact that they all have been previously determined to have immunogenic effects which make them useful for treatment of various types of tumors and/or cancer, (Compare In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)), we would note that the references which the examiner relies on would suggest that these materials, particularly the p53 derived protein of Levine and the IL-12 of Hall generate their respective effects in substantially different manners. Even given that these effects may both be classified as immunogenic effects, does not demonstrate that the prior art would regard them as both useful for the same purpose and in the same manner. We find nothing of record, and the examiner has pointed to no facts or evidence, which would suggest that these two diverse treatments would be useful in combination.

Thus, when we consider the claimed subject matter as a whole and the facts and evidence provided by the examiner, it is our conclusion that the examiner has failed to

Appeal No. 1999-1422
Application No. 08/408,915

provide sufficient basis on which to properly question the patentability of claims 1, 8, 11, 12, and 15 under 35 U.S.C. § 103. We, therefore, reverse this rejection.

In considering the remaining rejections of claim 2 as unpatentable over Levine, Paoletti, Hall and Nijman and claims 6, 7, and 13 as unpatentable over Levine, Paoletti, Hall and Livingston, it is sufficient to note that neither Nijman or Livingston provide that which we have determined to be missing from the combination of Levine, Paoletti and Hall. Therefore, we, also, reverse these rejections for reasons stated above.

SUMMARY

The rejection of claims 1, 2, 5 - 8, 11 - 13, and 15 under 35 U.S.C. § 112, first paragraph is reversed. The rejections of claims 1, 2, 5 - 8, 11 - 13, and 15 under 35 U.S.C. § 103 are reversed.

REVERSED

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DOUGLAS W. ROBINSON))
Administrative Patent Judge))
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)) BOARD OF PATENT
TONI R. SCHEINER)) APPEALS AND
Administrative Patent Judge))
)) INTERFERENCES
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DEMETRA J. MILLS))
Administrative Patent Judge))

Appeal No. 1999-1422
Application No. 08/408,915

FELFE AND LYNCH
805 THIRD AVENUE
NEW YORK, NY 10022

DWR/jlb