

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte WILLIAM R. MAJARIAN,
BRUCE A. D. STOCKER
and
SALETE M.C. NEWTON

Appeal No. 95-4700
Application 07/837,668¹

ON BRIEF

Before WINTERS, WILLIAM F. SMITH and LORIN, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 11, 21, 31, 34, 37 through 41, 56 through 61, 72, 73, and 75. As clarified in the Supplemental Examiner's Answer (Paper No. 43, July 10, 1996), claims 25 and 35 are

¹ Application for patent filed February 14, 1992. According to appellants, this application is a continuation of Application 07/348,430, filed May 5, 1989; which is a continuation-in-part of Application 07/190,570, filed May 5, 1988, now abandoned.

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pending and are allowed. Claim 31 is no longer rejected but is objected to as being dependent upon a rejected base claim but would be allowable if rewritten in independent form. Claim 1 reads as follows:

1. A recombinant gene comprising a nucleotide sequence which encodes a flagellin fusion protein, which protein comprises a flagellin sequence containing a first epitope of a flagellin structural gene with at least one epitope of a heterologous organism inserted within the flagellin sequence, wherein the flagellin protein is capable of binding to an anti-flagellin antibody.

The references relied upon by the examiner are:²

Asaka et al. (Asaka) 4,886,748 Dec. 12, 1989

Wei et al. (Wei), "Covalent Structure of Three Phase-1 Flagellar Filament Proteins of Salmonella," Journal of Molecular Biology, Vol. 186, pp. 791-803 (1985).

Eichinger et al. (Eichinger), "Circumsporozoite Protein of Plasmodium berghei :Gene Cloning and Identification of the Immunodominant Epitopes," Molecular and Cellular Biology, Vol. 6, No. 11, pp. 3965-72 (Nov. 1986).

Macnab, "Escherichia Coli and Salmonella Typhimurium: Cellular and Molecular Biology", American Society for Microbiology, pp. 70-83 (1987).

Dougan et al. (Dougan), "Live oral Salmonella vaccines: potential use of attenuated strains as carriers of heterologous antigens to the immune system," Parasite Immunology, Vol. 9, pp. 151-160 (1987).

Kuwajima, "Flagellin Domain That Affects H Antigenicity of Escherichia Coli K-12," Journal of Bacteriology," Vol. 170, No. 1, pp. 485-88 (1988).

² In addition, the examiner cited references to Tizard and Mandelstam at page 5 of the supplemental examiner's answer. However, the examiner did not include these references in a statement of any of the pending rejections. Nor did the examiner make a new ground of rejection in the supplemental examiner's answer which relied upon these references. Accordingly, we have not considered the Tizard and Mandelstam references. See In re Hoch, 428 F.2d 1341, 1342 n. 3, 166 USPQ 406, 407 n. 3 (CCPA 1970).

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Charbit et al. (Charbit), "Presentation of Two Epitopes of the preS2 Region of Hepatitis B Virus on Live Recombinant Bacteria," The Journal of Immunology," Vol. 139, No. 5, pp. 1658-64 (1987).

Kuwajima et al. (Kuwajima), "Presentation of an Antigenic Determinant From Hen Egg-White Lysozyme on the Flagellar Filament of Escherichia Coli," Bio/Technology, Vol. 6, pp. 1080-89 (1988).

Charbit et al. (Charbit), "Expression of a Poliovirus Neutralization Epitope at the Surface of Recombinant Bacterial: First Immunization Results," Ann. Inst.Pasteur/Microbiol., Vol. 139, pp. 45-58 (1988).

Ellis et al. (Ellis) PCT WO 86/00911 Feb. 13, 1986

Claims 1 through 3, 6, 7, 21, 37, 38, 72 and 73 stand rejected under 35 U.S.C.

§ 102(e) as anticipated by Asaka. Claims 4 and 5 stand rejected under 35 U.S.C.

103. As evidence of obviousness, the examiner relies upon Asaka, Macnab and Wei.

Claims 8 through 11 stand rejected under 35 U.S.C. § 103. As evidence of obviousness,

the examiner relies upon Asaka, Eichinger or Ellis. Claims 56 through 58 and 61 stand

rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon

Asaka, Charbit 1987 and Charbit 1988. Claims 59 and 60 stand rejected under 35 U.S.C.

§ 103. As evidence of obviousness, the examiner relies upon Asaka, in view of Charbit

1987 or 1988, Macnab and Wei. Claims 39 through 41 stand rejected under 35 U.S.C. §

103. As evidence of obviousness, the examiner relies upon Asaka in view of Charbit 1987

or 1988, Macnab, Wei and Dougan. In addition, claims 1 through 11, 21, 37 through 41,

56 through 61, 72 and 73 stand rejected under

35 U.S.C. § 112, second paragraph, as being indefinite.

We affirm the prior art rejections and reverse the rejection under 35 U.S.C. § 112, second paragraph.

DISCUSSION

1. Prior art rejections

In reviewing the “Replacement Brief on Appeal” (Paper No. 37, August 26, 1994) we note that appellants do not substantively argue the merits of the rejections under 35 U.S.C. § 103. Rather, appellants rely upon the arguments presented in regard to the anticipation rejection premised upon Asaka in support of the patentability of the claims rejected under 35 U.S.C. § 103. See page 4 of this paper. Furthermore, in regard to the rejection under 35 U.S.C. § 102(e), appellants have stated that “the claims can be grouped together.” See page 3 of this paper. Accordingly, the dispositive question in regard to the prior art rejections pending in this appeal is whether Asaka describes a recombinant gene as required by claim 1 on appeal?

We answer this question in the affirmative.

Claim 1 is directed to a recombinant gene which comprises a nucleotide sequence which encodes a flagellin³ fusion protein. In order to encode a fusion protein, the claimed recombinant gene requires two separate nucleotide sequences. The first is a “flagellin sequence containing a first epitope of a flagellin structural gene.” The second is one which

³ As explained on pages 7-11 of the supporting specification, flagellin is a structural protein in bacterial flagella.

encodes “at least one epitope of a heterologous organism.” As set forth in claim 1 on appeal, the second nucleotide sequence is “inserted within the flagellin sequence.” The fusion protein expressed by the recombinant gene must be “capable of binding to an antFLAGELLIN antibody.”

Asaka describes a nucleotide sequence denominated as the hag gene which codes for flagellin of E. coli. See Figure 1 of Asaka. As set forth in the paragraph bridging columns 2-3 of Asaka:

The present inventors remarked [sic] an excretion system of flagellin in investigating a system in which a target peptide is produced outside of a cell. Therefore, the whole base sequence of hag gene encoding flagellin was determined and the gene was inserted into a vector and then the hag gene on the vector was cut or a part of the gag gene on the vector was removed and into the resulting space is inserted linker DNA. Into the linker DNA in the vector is inserted DNA coding for a foreign peptide and the resulting vector is introduced into bacteria. As a result, the foreign peptide is excreted from the bacteria as a fused peptide with flagellin. Under certain condition the excreted peptide forms flagella, which facilitates the recovery of the peptide. Moreover, it may be possible that some foreign peptides which could not be secreted from bacteria by conventional secretion systems are excreted by this excretion system.

As can be seen, Asaka describes a recombinant gene formed by inserting DNA coding for a foreign peptide into a flagellin gene.⁴ Use of the entire hag gene as taught by Asaka will necessarily result in the recombinant gene containing “a first epitope of a flagellin structural gene.” The foreign DNA inserted within the flagellin gene in Asaka may be a synthesized polynucleotide encoding hepatitis B virus (HBV) surface antigen. See column 29, line 51-column 30, line 26 of Asaka. As stated at column 30, lines 22-26:

These strains excrete flagellin fused with peptide
LeuValLeuLeuAspTyrGlnGlyMetLeuProValGysProLeuGly
encoded by the synthesized DNA (Hbs-Ag-IV) which is
inserted in the plasmid and form flagella.

A recombinant gene according to Asaka which comprises a complete hag gene into which has been inserted a synthesized polynucleotide sequence encoding HBV surface antigen is within the scope of claim 1 on appeal. On this basis, we find no error in the examiner's determination that Asaka anticipates claim 1 on appeal.

We have carefully considered the argument presented by appellants on appeal on pages 3-4 of the Replacement Brief on Appeal in regard to the anticipation rejection. However, it is unclear what point appellants are trying to make. Asaka clearly and unambiguously describes a recombinant gene which is constructed from a complete flagellin gene into which foreign DNA has been inserted. It appears to be beyond argument that such a recombinant gene would contain “a first epitope of a flagellin

⁴ In similar fashion, the present invention can use linkers to insert foreign DNA into a flagellin gene. See page 33, lines 2-18, of the supporting specification.

structural gene” as required by claim 1 on appeal. The fusion protein encoded by such a recombinant gene would expectedly be “capable of binding to an antflagellin antibody,” as also required by claim 1 on appeal. On this record, it is incumbent upon appellants to establish that a full length flagellin gene into which has been inserted a second nucleotide sequence encoding an antigenic peptide, such as HBV surface antigen, as described by Asaka does not fall within the scope of claim 1 on appeal. Appellants have not done so.

As explained above, our determination that Asaka anticipates claim 1 on appeal is dispositive of all of the prior art rejections pending in this appeal. Consequently, all of the prior art rejections are affirmed.

2. Rejection under 35 U.S.C. § 112, second paragraph.

This rejection is set forth in the paragraph bridging pages 12-13 of the Supplemental Examiner's Answer.⁵ The examiner indicates that the claims are not clear as to the metes and bounds of the phrase “a first epitope of a flagellin structural gene.” However, the examiner has not established that for a given flagellin nucleotide sequence one skilled in the art would not be able to readily discern whether that nucleotide sequence encodes a protein which is antigen, i.e., contains an epitope. Without a more

⁵ The page numbers which appear in the upper right-hand corner of this paper beginning on page 6 are incorrect.

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comprehensive fact-based analysis from the examiner, we do not find that the examiner has discharged her initial burden of establishing reasons why the claims on appeal are indefinite.

The rejection under 35 U.S.C. § 112, second paragraph, is reversed.

The decision of the examiner is affirmed.

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

AFFIRMED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
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WILLIAM F. SMITH)	BOARD OF PATENT
Administrative Patent Judge)	APPEALS AND
)	INTERFERENCES
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