BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

A		B		C	X

File Number: W 23/91 - 3.3.2

Application No.: PCT/US90/06292

Publication No.: WO9108291

Title of invention: Latency associated peptide and uses therefor

Classification: C12N 15/16

D E C I S I O N
of 8 September 1992

Applicant: Genentech, Inc.

Headword: Latency associated peptide/GENENTECH

PCT Article 17(3)(a), Rules 13 and 40

Keyword: "Lack of unity 'a posteriori' - no examination of inventive step in cases that are not clear - non-unity not established - refund of additional search fee"

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number : W 23/91 - 3.3.2
International Application No. PCT/US90/06292

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 8 September 1992

Applicant : Genentech, Inc.
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Subject of the Decision : Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fee) of the European Patent Office (branch at The Hague) dated 11 March 1991.

Composition of the Board :

Chairman : P.A.M. Lançon
Members : U. Kinkeldey
R. Schulte

Summary of Facts and Submissions

I. The Applicants filed an international patent application PCT/US90/06292 with 51 claims.

II. The EPO acting as an International Search Authority (ISA) sent to the Applicants an invitation to pay one additional search fee pursuant to Article 17(3)(a) and Rule 40.1 PCT.

III. Claim 1 reads as follows:

"1. An isolated nucleic acid sequence comprising a sequence that encodes a latency associated peptide having a molecular weight of about 75,000 when measured by non-reducing SDS-page and capable of antagonizing a biological activity of mature TGF-ß, provided that the sequence does not also encode a mature TGF-ß."

Dependent Claims 2 to 8 relate to further embodiments of the nucleic acid sequence, an expression vector comprising the nucleic acid sequence and a host cell transformed with the expression vector.

Claim 9 is an independent substance claim and relates to an isolated DNA sequence worded more generally than that of Claim 1.

Following Claims 10 to 26 relate to certain embodiments of the sequences, expression vectors, host cells and methods of producing the latency associated peptide by expression of the nucleic acid in the host cell culture in a similar fashion to that of the claims dependent on Claim 1.

Independent product Claim 27 reads as follows:

"27. Latency associated peptide that is completely free of source proteins."

This independent claim, again, is followed by dependent claims relating to pharmaceutical compositions comprising certain preferred embodiments, and certain methods of application of the pharmaceutical composition.

In particular, Claim 29 relates to a pharmaceutical composition useful for antagonising a TGF-ß activity comprising a therapeutically effective amount of the peptide of Claim 27 and Claim 51 relates to a method for diagnosing the presence of a condition detectable by the presence of mature TGF-ß in serum of a patient comprising adding to the serum a labelled form of the peptide of Claim 27.

IV. With regard to non-unity the ISA found inter alia the following:

"For patent applications claiming several new uses of a product in essentially different areas and/or new processes concerning the product (e.g. preparation, etc), there is a common inventive concept if the product is new.

On the other hand when the product is known, the claims for this different categories are no more linked, and consequently there is no common inventive concept.

As seen on the search report (EP-A-0 293 785 and FEBS lett., Vol. 242, p. 240-244), LAP is not a new product.

Therefore the different uses of LAP do not have a common inventive concept, and the application lacks unity of invention according to Rule 13.1 PCT."

For these reasons, the ISA identified the following groups of invention:

(1) Claims 1 to 28, 51: nucleic acids encoding LAP, LAP as a pure product and its use in diagnostics of TGF-ß;
(2) Claims 29 to 33, 42 to 44: the use of LAP in pharmaceutical compositions.

V. The Applicants paid the fee under protest. In support of the protest the Applicants submitted that they disagreed with the search examiners characterisation of the FEBS letts. article cited in the search report as teaching LAP. As stated on page 4, lines 17 to 25 of the present international application, the 39 Kd sub-unit of the masking protein reported by the FEBS letts. article was found to have no masking activity, leading the authors to conclude on page 243 that the 180 to 210 Kd component is the minimum active unit for masking TGF-ß. Thus, it was not clear that the 39 Kd sub-unit is indeed LAP, since it does not have the activity of LAP reported in the present international application and in Claim 1, namely being capable of being antagonising a biological activity of mature TGF-ß.

Reasons for the Decision

1. The protest is admissible.

2. The invitation by the ISA to pay an additional search fee is based on the finding that, within the meaning of

Article 17(3)(a) PCT there is a lack of a unifying inventive concept, because the common link for all claims, and in particular for Claims 29 and 51 relating to a composition in the field of therapy and to a method for diagnosing respectively, namely the protein LAP was said to be known in the light of two cited prior art documents. The finding, thus, is based on an a posteriori judgment.

3. In the decision G 1/89 (OJ EPO 1991, 155) the Enlarged Board of Appeal concluded that the ISA is entitled to raise an a posteriori objection as to non-unity, i.e. based on the disclosure of documents found during the international search; at the same time, however, the decision held, that any statements as to novelty and inventive step can only have a preliminary character and that, therefore, only in clear cases an objection should be raised; further fair treatment to the Applicants was proposed.

4. One may agree to the ISA's statement put down in its invitation that novelty of a certain product may justify claims of different categories to be contained in one single application without contravening the requirement of unity of the invention. In the present case the two independent product Claims 1 and 27, (see above paragraph III) relate to two "products", namely a nucleic acid sequence and the protein relating to the nucleic acid sequence. These products might constitute the common link if they were novel.

5. The Board carried out a preliminary examination of novelty of Claims 1 and 27 in the light of the two prior art documents mentioned by the ISA in its search report and comes to the result that document EP-293 785 does not disclose an isolated nucleic acid sequence that encodes a latency associated peptide of having a molecular weight of

about 75,000, capable of antagonising a biological activity of mature TGF-ß wherein the sequence does not also encode a mature TGF-ß. The disclosure of this document relates mainly on the cloning and expression of a recombinant TGF-ß1 in its mature form. The mature TGF-ß is expressis verbis excluded from Claim 1 of this international patent application. If in EP-293 785 precursors of the mature TGF-ß1 are disclosed they do not relate to DNA sequences that encode a latency associated peptide having a molecular weight of about 75,000. None of the proteins described in this document is reported to be capable of antagonising a biological activity of TGF-ß. On the face of it, after this preliminary examination of novelty, thus, Claims 1 and 27 may be considered as not being anticipated by this document.

6. The second document cited by the ISA (see above paragraph IV) does not disclose any DNA sequence at all. The disclosure relates to a protein which reversibly mask TGF-ß activity, named "masking protein" (MP). The purification of MP was reported and it was shown that the smaller of the two sub-units of MP was identical to the N-terminal part of the TGF-ß precursor. On page 243, right column, lines 7 to 19, it is disclosed that TGF-ß was composed of at least three components, namely a monomer of 12.5 kDa, and MP sub-units of 39 kDa and 105 to 120 kDa. These two MP sub-units formed a complex of 180 to 210 kDa in which 39 kDa sub-units were linked with the 105 to 120 kDa component by disulfide bonds. The 39 kDa sub-unit was reported not to have any activity. The 180 to 210 kDa component was thought to be the minimum active unit for masking the TGF-ß. Although this disclosure provides a step forward in the definition of the sub-unit of TGF-ß which could possibly be responsible for the masking effect it seems not to be, on the face of it, a clear and unambiguous disclosure of the latency associated peptide

having a molecular weight of about 75,000, let alone the corresponding isolated nucleic acid sequence as claimed in Claim 1.

7. It follows from the above that novelty of none of the two independent product Claims 1 and 27 (see paragraph III above) is at issue.

8. For a final decision on unity, depending on the patentability of product Claims 1 and 27, it would now be necessary to examine whether these claims fulfil the requirement of an inventive step. The Board refrains from doing so because the present case is not at all a clear case, as required by the decision of the Enlarged Board of Appeal (see above point 3) nor would the Board give the Applicant a fair treatment as required in the same decision, when taking into account the facts of the present case as is the technical field, the state of the art cited by the ISA, the prior art cited in the international patent application and the fact that any non-unity considerations under the PCT are made without the Applicants having had an opportunity to react by amending claims. Thus, the Board exercises restraint in the assessment of inventive step and refrains from considering the application as not complying with the requirement of unity of invention on the ground of lack of inventive step as the ISA should have done, if it had arrived at the examination of an inventive step of the nucleic acid sequence as claimed in Claim 1.

9. Since for the above reasons the ISA should have refrained from its invitation to pay an additional fee the invitation has no legal effect and thus the conditions of Rules 13.1 and 13.2 PCT are fulfilled. The additional fee, therefore, has to be reimbursed.

Order

For these reasons, it is decided that:

Refund of the additional search fee is ordered.

The Registrar: The Chairman:

P. Martorana P. Lançon