BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Publication in the Official Journal [redacted] / No

File Number: T 711/89 - 3.3.2

Application No.: 83 301 208.1

Publication No.: 0 088 622

Title of invention: Animal interferons, processes involved in their production, compositions containing them, DNA sequences coding therefor and expression vehicles containing such sequences and cells transformed thereby

Classification: C12N15/00

D E C I S I O N
of 4 March 1992

Applicant: GENENTECH, INC.

Headword: Animal interferons/GENENTECH

EPC Articles 82 and 123(2)

Keyword: "Amended claims - added subject-matter (no)"
"Unity of invention - single general inventive concept (yes)"

Headnote

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number : T 711/89 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 4 March 1992

Appellant : GENENTECH, INC.
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Decision under appeal : **Decision of Examining Division of the European Patent Office dated 13 June 1989, and posted on 18 July 1989, refusing European patent application No. 83 301 208.1 pursuant to Article 97(1) EPC.**

Composition of the Board :

Chairman : P.A.M. Lançon
Members : A.J. Nuss
E.M.C. Holtz

Summary of Facts and Submissions

I. European patent application No. 83 301 208.1 (publication No. 0 088 622) was refused by a decision of the Examining Division on the basis of objections raised under both Articles 123(2) and 82 EPC against three alternative sets of claims corresponding to Appellant's main and auxiliary requests 1 and 2.

(i) In the reasons for the Decision the Examining Division started by noting "that Claim 12 in the present form avoids a novelty objection with respect to the document WO-A-80 023 75 (i.e. document (A) in the present decision) which discloses purified bovine leukocyte interferon". Furthermore, there was no need to go into the question of novelty and inventive step of the matter claimed in accordance with all requests because of the other objections which form the basis of the present decision.

(ii) The Examining Division then rejected the main and first auxiliary request under Article 123(2) EPC. It considered that Claims 8 and 19 of the corresponding versions of claims related to subject-matter not directly and unambiguously derivable from the application as filed. In particular, the statement on page 10, last paragraph of the application as filed was not considered to constitute a sufficient basis for allowing said claims because a selection was made whereby new matter was generated.

(iii) In addition, a non-unity objection was raised against the claims on file whereby the following separate inventions were made out in the

claims according to the main and first auxiliary request:

(a) bovine leukocyte interferons and method and means for producing them by recombinant DNA techniques (Claims 1 and 12 and partially Claims 4-7, 9-11- 15-18);

(b) bovine fibroblast interferons and method and means for producing them by recombinant DNA techniques (Claims 2 and 13 and partially Claims 4-7, 9-11, 15-18);

(c) bovine immune interferon and method and means for producing it by recombinant DNA techniques (Claims 3 and 14 and partially Claims 4-7, 9-11, 15-18);

(d) non-human interferons and method for their production (Claims 20-22);

(e) method for the production of interspecies or interfamily hybrid interferons (Claims 8, 19, 23-24 and partially Claims 9-11).

In view of the deletion of Claims 8 and 19 to 24, the second auxiliary request was considered to cover only the groups of inventions (a), (b), and (c).

Since each of the five inventions related to different technical problems and to different solutions thereto, they could not be considered to be so interrelated as to form a single general inventive concept.

In addition, the Examining Division pointed out that in US-A-4 262 090, i.e. document (E), a general strategy for

preparing CDNAs coding for mammalian interferons had been outlined. Further documents were cited to illustrate the isolation of various non-human interferons, the preparation of human interferons by recombinant DNA techniques and the general strategies for DNA cloning. For each of the three types of bovine interferon a different probe had to be used. Therefore, the same known experimental approach was used in three different situations with the result that three known products of fundamentally different nature were obtained. Not only the claims relating to (a) bovine **leukocyte**, (b) bovine **fibroblast** and (c) bovine **immune** interferon, but also those to (b) **non-human** interferons actually concerned distinct inventions which could not be claimed together in the same application. In addition, the further technical development of these inventions in view of the creation of hybrid interferons, (i.e. **interspecies** or **interfamily** hybrid interferons) appeared to be only partially related to the said four parallel inventions (a) - (d). This latter invention, i.e. invention (e), should therefore also be claimed separately.

II. The Appellant lodged an appeal against the decision to refuse the European application.

III. In accordance with Article 4 of the Rules of Procedure of the Boards of Appeal, the Rapporteur issued a communication in which a provisional opinion was given on both the issues of added subject-matter under Article 123(2) EPC and that of unity of invention under Article 82 EPC.

IV. Oral proceedings took place on 4 March 1992, at the beginning of which the Appellant submitted a revised set of claims (see point V below).

The arguments put forward by the Appellant in the course of the written proceedings and/or oral proceedings were essentially the following:

(i) The present claims are all supported by the application as originally filed. In particular the claims relating to hybrid, interspecies and intrafamily interferon are based on the disclosure on page 10 of the application, which is nothing else than an invitation to the ordinary skilled reader to construct a hybrid animal interferon (IFN) as including, as its immediate embodiment, an intrafamily hybrid of bovine interferons (BoIFNs), since this is the species for which DNA and amino acid sequence data, not to mention test data, are given in the description. The next immediate embodiment would be one which employed a BoIFN fragment with an IFN fragment of another species, i.e. an interspecies hybrid.

Moreover, the reference "taking advantage of common restriction sites" at the foot of page 10 is identifying an approach to the manipulation of the DNA to join the different fragments. As indicated, this is "according to known methods". There should not be any dispute that the skilled person would by this means, or by any other means known in the art for joining DNA, have joined the fragments. Moreover, in view of the relatively high level of DNA homology between the sequences coding for the individual IFN members, common restriction sites should not be at all hard to find. Furthermore, additional restriction sites can be obtained by altering the DNA. Consequently, the subject-matter of the refused claims is not based on a selection as alleged by the Examining Division.

(ii) The present invention is based on the discovery and practical utilisation of interspecies nucleotide hybridisation in the cloning of non-human IFNs. Although in the present application different probes are used for the different BoIFNs, the approach is the same, and that constitutes a common inventive concept. What the invention has established generically, therefore, is the applicability of interspecies DNA probing for identifying and cloning of IFN DNA of animals the human IFN DNA being already known. The question of unity of invention therefore seems to come down to merely a consideration as to whether each of the claims incorporates that common inventive methodology, either explicitly or implicitly, as an essential feature. However, the bovine DNA sequences specified the present application, and referred to in the present claims, inherently and implicitly embody the present methodology, because that is how they were arrived at. The fact that they are different substances can have no overriding bearing on the question of unity of invention.

Finally, document (E) neither anticipates not renders obvious the present invention. There is no disclosure for believing that it places any cloned animal IFN DNA in the state of the art. It only deals with the supposed increase in the output of IFN in mammalian cells by crossing a natural cell with a mutant cell.

V. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the set of claims submitted during the oral proceedings (Claims 1 to 27). He declared that all other requests earlier on file were thereby withdrawn.

The present independent or new Claims read as follows:

1. A process for identifying DNA encoding an interferon of a non-human animal species, which comprises preparing a library of cloned DNA from said species and probing it with a hybridisation probe of interferon DNA from a different species, and analysing positive clones for interferon-encoding sequences.

3. Non-human animal interferon encoding DNA as identifiable by the process of Claim 1 or Claim 2.

4. DNA according to Claim 3 encoding a avian, bovine, canine, equine, feline, hircine, ovine, piscine or porcine interferon.

5. DNA according to Claim 3 encoding a non-human animal interferon selected from bovine leukocyte, fibroblast and immune interferon.

6. DNA according to Claim 5 encoding bovine leukocyte interferon.

7. A process for obtaining DNA encoding a hybrid interferon which comprises ligating a fragment of DNA according to any one of Claims 3-6 which fragment does not encode an entire interferon polypeptide with one or more DNA fragments encoding complementary part or parts of an interferon of another member of the same family and of the same animal species and/or of the same or another member of the same family but of a different species.

8. A process which comprises producing a non-human animal or hybrid interferon having an amino acid sequence encoded by DNA of any one of Claims 3 to 7, the process comprising the expression in a recombinant host cell of DNA encoding said interferon.

16. A process according to Claim 8 wherein there is produced an interspecies or intrafamily hybrid interferon containing a portion of at least one of the bovine leukocyte interferons depicted in Figures 3a-d hereof, or a portion of at least one of the bovine fibroblast interferons depicted in Figure 13 hereof, with complementary part or pats of an interferon of another member of the same family and of the same animal species and/or of the same or another member of the same family but of a different species.

17. A DNA isolate comprising a sequence coding for an interferon of any one of Claims 9-16.

18. An expression vector operably harbouring a DNA sequence coding for an interferon of any one of Claims 9-16.

19. A cell transformed with an expression vector of Claim 18.

20. A bovine leukocyte interferon comprising an amino acid sequence from that depicted in any of Figures 3a-d hereof and devoid of glycosylation.

21. A bovine fibroblast interferon comprising an amino acid sequence from that depicted in any of Figures 9a-c hereof.

22. A bovine immune interferon comprising an amino acid sequence from that depicted therefor in Figure 13 hereof.

27. An interspecies or intrafamily hybrid interferon containing a portion of at least one of the bovine leukocyte interferons depicted in Figures 3a-d hereof, or a portion of at least one of the bovine fibroblast interferons depicted in Figures 9a-c hereof, or a portion of the bovine immune interferon depicted in Figure 13 hereof, with complementary part or parts of an interferon of another member of the same family and of the same animal species and/or of the same or another member of the same family but of a different species.

Reasons for the Decision

1. The appeal is admissible.

Amendments

2. The present claims correspond to those considered by the first instance with the exception of Claims 1, 4 to 6 and 8, whereby the present Claims 16 and 27 correspond to the refused Claims 8 and 19 (several claims directly or indirectly referred back to the objected claims).

- Claim 1 differs from previous Claim 20 in that the claim now relates to a process for identifying DNA encoding an interferon of a non-human animal species instead of one for obtaining said interferon. This claim is adequately supported by the application as originally filed (see page 1, lines 15/16; page 11, lines 1 to 4; page 21, line 19 ff, in particular sections A to G).

- Claims 4 to 6 are new claims introduced at the appeal stage. They are based on subject-matter originally disclosed in the application (see page 1, lines 15/16; page 10, lines 15 to 21; page 11, lines 1 to 4 and line 18 ff; page 21, line 19 ff, in particular sections G, K and M).

- Claim 8 differs from previous Claim 24 in that it now also covers a process which comprises producing a **hybrid interferon**, whereas Claims 16 to 27 relate to **interspecies or intrafamily hybrid interferon**. In view of the objections raised by the first instance, the question arises whether these three claims are adequately supported by the original disclosure.

All the examples included in the present application concern the preparation of bovine interferons. In view of this fact and the information provided at the bottom of page 10 of the application, the Board is convinced that the man skilled in the art would immediately realize that the further teaching contained in the application, viz. to provide interspecies and intrafamily hybrid interferons by taking advantage of common restriction sites within the genues of the various animal interferons and recombining corresponding portions, must necessarily apply to the bovine interferons described in the examples. Moreover, it is also clear from different statements made in the description that with the present invention other animal interferons can be obtained, in particular those normally endogenous to animals of the avian, bovine, canine, equine, feline, hircine, ovine, piscine, and porcine families.

Under these circumstances, the Board considers that the subject-matter of the claims in question cannot be said to be based on a selection by which new matter is generated.

- The remaining Claims 2, 3, 7, 9 to 15 and 17 to 26 correspond to Claims 21, 22, 23, 1 to 7 and 9 to 18 already considered by the Examining Division. The Board can see no formal objection to these claims either.

It follows from above, that the present Claims 1 to 27 are all acceptable under Article 123(2) EPC.

Unity of invention

3. When dealing with the question of unity of invention, it is imperative to note that, according to Article 82 EPC, a European patent application may relate to a group of inventions so linked as to form a simple general inventive concept. The unity of invention can therefore be objected to in all cases where the binding element between a group of inventions, i.e. the single general inventive concept, is destroyed, be it in consequence of lack of novelty or inventive step. This leads the Board to the two most relevant documents to be considered when dealing with the question of unity of invention of the present invention, i.e. document (A) and (E) (see point I (i) and (iii)).

4. (i) Since document (E) is the only of the two documents which concerns the preparation, via recombinant DNA technology of various mammalian interferons, the Board considers that this document is the closest state of the art.

As can be seen from the claims, the main object of this document concerns a method for producing mRNA specific for mammalian interferon in amounts sufficient to be useful for formation of recombinant DNA capable of transformation of microorganisms to form transformants, which are capable of replication

of said recombinant DNA and expression of ds cDNA derived from said mRNA, said method comprising fusing intra- or inter-specifically a mammalian cell semi-constitutive for interferon with a mammalian cell which is wild type for interferon to produce hybrid cells; inducing the hybrid cells to over-produce mRNA specific for interferon, and isolating the overproduced mRNA. In addition, the description contains general instructions relating to the preparation of IFN cDNA, IFN dsDNA and recombinant DNA. Under the heading "Preparation of cDNA from IFN mRNA", it is said that the obtained dC-tailed ds cDNA is preparatively electrophoresed on a gel and the desired base pair region (~200-500 base pairs) cut out of the gel and electrophoretically eluted into a dialysis bag. The eluted material is extracted, concentrated by lyophilization and precipitated. After centrifugation, the dC-tailed ds cDNA is redissolved in annealing buffer (see column 11, line 43 to column 12, line 52). The further steps relate to transformation and identification of suitable clones. It is also said in this document that by this method various mammalian interferons may be produced, such as murine IFN, interferon for domestic animals, e.g. equine, bovine, canine, feline etc. It is to be noted that in this list no specific interferon, like leukocyte or fibroblast IFN, is quoted in relation with non-human IFNs (see column 4, line 36 to column 5, line 30).

(ii) In the course of the appeal proceedings, the Appellant referred to his previous submissions, made in a letter dated 15 July 1986, in order to support the view that document (E) should not be considered as an enabling disclosure. The Board does not exclude that this question could become highly relevant at a

later stage of the proceedings. Be that as it may, what actually matters is that document (E) prima facie does not disclose any process for obtaining identifiable non-human animal encoding DNA which could be regarded as causal for the obtaining of a concrete animal IFN such as leukocyte, fibroblast or immune interferon. It is thus possible to establish a major difference between the claimed invention and that described in document (E) without having to deal with the question of enabling disclosure of this prior art.

5. Under these circumstances, the problem vis-a-vis the closest state of the art can be seen in the provision of a general means for obtaining desired particular non-human animal IFNs such as bovine leukocyte interferons.

The claimed solution is not confined to the provision of a general process (Claim 8) and its particular embodiments in the form of depending processes for obtaining the most desired IFNs (Claims 9 to 16). It necessarily also covers the provision of the corresponding genetic precursors as embodied by the identified and isolated DNA sequence (Claims 17 and 3 to 6) as well as the processes required for such identification and isolation (Claims 1, 2 and 7), including the means for using them in the form of an expression vector and a transformed cell (Claims 18 and 19) and, of course, also the most desired particular interferons per se (Claims 20 to 27).

Claims 3 and 8 manifestly implement the broadest possible solution of the problem to be solved as they provide the generally applicable process and the DNA coding for non-human animal IFN, i.e. the precursor necessary for obtaining the desired interferon.

In virtue of Article 82 EPC already mentioned, no flaw can be detected in respect of the requirement of unity of invention when looking at the different aspects of the solution in the way set out above. In the present case, the problem and its solution are the illustration of a single inventive concept unifying the different aspects of the claimed invention. As long as the object of Claims 3 or 8 is not destroyed on the basis of lack of novelty or inventive step, there can be clearly no reason to object to the unity of invention.

6. It can be seen from point I (i) above that the Examining Division had apparently good reasons for not maintaining the novelty objection against previous Claim 12 (present Claim 20) on the basis of document (A). For the rest, it is stated in section VI of the contested decision that "the question of novelty and inventive step of the matter claimed in all requests needs not to be gone into because of the other objections which form the basis of the present decision". There can thus be no doubt that, in the contested decision, the assessment of unity of invention under Article 82 EPC had not been carried out in accordance with the principles set out in the preceding paragraphs. Consequently, the Examining Division has not shown that in the prior art the above stated problem had already found a solution liable to destroy the common inventive concept unifying the claims of the present invention.

The "separate inventions" made out in the contested decision represent actually nothing more than a misleading classification of the claims on the basis of the different interferons to be produced, without having shown before that there is no single general inventive concept, or that such concept has been destroyed on the basis of some relevant state of the art, such classification is simply

meaningless and therefore of no use for deciding whether the claims meet the requirements of Article 82 EPC or not.

Under these circumstances, the Board can only conclude that there is no valid basis for challenging to unity of invention of the present invention. As the Examining Division will have to complete the examination of the claims, at least on novelty and inventive step, the Board of Appeal should not anticipate this examination by carrying out of its own motion investigations in this respect.

7. It follows from the preceding paragraphs that the present claims do not give rise to objections under Articles 123(2) and 82 EPC.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Examining Division for further prosecution on the basis of the set of claims submitted during the oral proceedings.

The Registrar: The Chairman:

P. Martorana P.A.M. Lançon

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