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D E C I S I O N
of 14 February 2002

Case Number: T 0111/00 - 3.3.4

Application Number: 92901508.9

Publication Number: 0679186

IPC: C12N 15/19

Language of the proceedings: EN

Title of invention:
Monokine MIG induced by IFN-GAMMA

Applicant:
FARBER, Joshua Marion

Opponent:
-

Headword:
Monokine/FARBER

Relevant legal provisions:
EPC Art. 56

Keyword:
"Inventive step (no)"

Decisions cited:
T 0296/93, T 0333/97

Headnote/Catchword:
-

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Case Number: T 011/00 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 14 February 2002

Appellant: FARBER, Joshua Marion
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 11 January 1999 refusing European patent application No. 92 901 508.9 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairwoman: U. M. Kinkeldey
Members: F. L. Davison-Brunel
C. Holtz

Summary of Facts and Submissions

I. The appeal lies from the decision of the Examining Division to refuse the European patent application No. 92 901 508.9 (international publication No. WO 92/10582) with the title "Monokine Mig induced by IFN-Gamma".

The claim request which served as a basis for the decision of the Examining Division comprised claims 1 to 11, 14 to 21 filed on 19 September 1996 as well as claims 12 and 13 filed on 26 July 1997.

Claim 1 read as follows:

"1. An intron-free DNA molecule encoding a mammalian monokine induced by gamma interferon (MIG) which is at least 90% identical to a second DNA molecule having a nucleotide sequence as shown in

SEQ ID NO: 4

(*there follows SEQ ID NO:4 as shown on page 32 of the patent application*)."

Claims 2 and 3 related to further features of the DNA of claim 1. Claims 4 and 5, 6 to 8 respectively related to proteins encoded by, and host cells containing said DNA. Claims 9 to 11, 15 to 18 were addressed to methods of producing a mammalian MIG protein. Claims 12 to 14 were addressed to nucleotide probes. Claims 19 to 21 related to a composition comprising antibodies immunoreactive with a specific human MIG but not with a specific mouse MIG, both being identified by their sequences.

The Examining Division came to the conclusion that the subject-matter of claim 1 was obvious in view of the teachings of the prior art document:

(1): Farber,J.M., Proc.Natl.Acad.Sci.USA, Vol. 87, pages 5238 to 5242, July 1990

which disclosed a mouse monokine induced by gamma interferon (γ-IFN).

II. The arguments in writing by the Appellant (Applicant) may be summarized as follows:

Document (1) disclosed a DNA sequence which had only 78% identity with the DNA sequence of the claimed human MIG (SEQ ID NO:4) and the role of the corresponding protein was qualified in a speculative manner: "**may** be a cytokine", "**suggest** that... it is neither identical to nor the mouse homologue of any member of the PF4 family", "**may** have a role ...specific to IFN-γ".

The skilled person would want stronger evidence of the role of the protein before committing ressources to try to find other related proteins.

The document

(2): Linzer, D., Human Cytokines: Handbook for Basic and Clinical Research III, Eds. Bharat B. Aggarwal, Blackwell Sc., Chapter 9, pages 166 to 188, 1998

detailed the uncertainty that human homologues of some mouse cytokines, in this case proliferin, even existed. It would have been by no means expected that a human homologue to the mouse protein disclosed in

document (1) could be isolated. There was only a hope to succeed in finding such an homologue but no reasonable expectation of success to do so.

Furthermore, had the skilled person decided to look for human MIG DNA sequences on the basis of the mouse MIG DNA sequence shown in document (1), he/she would not have reasonably expected to identify the DNA sequence **specifically** claimed.

For all these reasons, the subject-matter of claim 1 was to be considered inventive.

III. The Appellant requested that the decision under appeal be set aside. He also requested interlocutory revision under Article 109 EPC. Oral proceedings were not requested.

Reasons for the Decision

Procedural matter

1. The Appellant's request for interlocutory revision under Article 109(1) EPC was not allowed by the Examining Division, which consequently remitted the case to the Board of Appeal under Article 109(2) EPC. The Appellant did not request oral proceedings and, therefore, the case may be decided without summoning them. Since the case can be decided on the basis of the grounds and facts already discussed in the first instance, there is no need to hear him further (Articles 113 and 116 EPC).

Substantive matter:

Inventive step of claim 1

2. The closest prior art is document (1) which describes the isolation from a monocyte/macrophage cell line, of a cDNA encoding a mouse cytokine which is induced by γ-IFN (m119). m119 is reported to be a member of the platelet factor 4 (PF4) family of cytokines. Its sequence and that of the encoding cDNA are shown in Figure 3. It is stated on page 5242 that m119 is **not** the homologue of any of the then known human cytokines of the PF4 family. The purpose of studying cytokines is identified as being an interest in investigating the potential therapeutic value of such macrophage products "*because of the wide involvement of macrophages in processes relevant to* ***human*** *health and disease*".(page 5238, right-hand column, emphasis added)

3. Starting from the closest prior art, the problem to be solved can be defined as the provision of further cytokines induced by γ-IFN.

4. The solution provided by claim 1 is cDNAs encoding cytokines having at least 90% identity to the specific cDNA of a **human** cytokine identified by its sequence (SEQ ID NO:4). The claim comprises this last cDNA which, according to the specification of the application, was isolated by hybridisation of the m119 cDNA of document (1) as a probe to a cDNA library made from a human monocyte cell line treated with γ-IFN.

5. In the Board's judgment, the statements in document (1) relating to the potential therapeutic value of human cytokines and to the fact that no human homologue to the newly isolated cytokine was to be found amongst the already known human cytokines would give the skilled

person an incentive to look for this human homologue. The Appellant's argument to the contrary on the basis of the alledgedly speculative role of m119 as described in document (1) is not found convincing. It is indeed stated in document (1) that "*the m119 protein **may be** a cytokine that affects the growth, movement or activation state of cells that participate in immune and inflammatory responses*" (abstract), and that "*the sequence comparison **suggests** that although related to these other members of the (PF4) family, m119 is neither identical to nor the mouse homolog of any of those described.*" (page 5242, left hand column) and that "*...the MIG protein **may have** a role in those effects on macrophages specific to IFN-γ*" (page 5242, left-hand column; emphasis added). Yet, none of these statements sheds doubts on the fact that m119 **is** a cytokine, which fact is anyhow disclosed *expressis verbis* on page 5238, right hand column: "*In this report, I describe the analysis of a cDNA of an mRNA that is selectively induced by IFN-γ and that encodes **a member of the PF4 family of cytokines.***" (emphasis added). They only reflect the author's thoughts as to which of the many roles attributable to cytokines in general may be that of the newly isolated cytokine. As such, they cannot distract the skilled person from the above mentioned incentive.

6. It is readily apparent from Example 5 of the application that the isolation of the human cytokine cDNA was carried out in a straightforward manner making use of the m119 cDNA described in document (1) as a probe for the selection of the relevant cDNA clones. The claimed cytokines cannot, therefore, derive inventive step from the way they were isolated.

7. In this respect, it must be noted that the approach of "reasonable expectation of success" as developed in the

case law of the Boards of Appeal starting from decision T 296/93 (OJ EPO 1995, 627) does not apply here. This approach is intended to take into account the complexity inherent to some recombinant DNA techniques, which may jeopardize the final outcome of experiments making use of them (see decision T 333/97 of 5 October 2000; point 13). In the present case, the skilled person would have considered the cloning of the human cDNA as a matter of routine since the necessary probe was available from document (1) and, indeed, as already mentioned, no problems were encountered.

8. The Appellant argued on the basis of document (2) which discloses that no human homologue to mouse proliferin had been identified, that the skilled person could not know whether or not the human homolog to m119 existed. It must, however, be noticed that document (2) was published eight years after the priority date of the application in suit. Its teachings are, thus, not relevant to evaluate the skilled person's state of mind at that date.

9. Finally, the argument was presented that the skilled person could not expect the specific sequence (SEQ ID NO:4) of the cloned cDNA and that, in that sense, the sequence per se was inventive. However, the subject-matter of claim 1 is not SEQ ID NO:4 but sequences which are 90% identical to it and so the argument does not apply. Admittedly, the cDNA having the sequence identified as SEQ ID NO:4 is comprised within claim 1. In this respect, the Board's findings are that a specific DNA sequence must be composed of a succession of defined deoxyribonucleotides, whichever this is and that, therefore, it cannot be considered inventive for

this sole reason. Inventive step could be acknowledged if the specific succession of deoxyribonucleotides imparted some unexpected properties to the molecule, which was never argued to be the case.

10. For the reasons given in points 4 to 6 and 8 above, inventive step is denied.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona U. Kinkeldey