BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [ ] To Chairmen and Members
(C) [X] To Chairmen
(D) [ ] No distribution

D E C I S I O N
of 25 June 2004

Case Number: T 0150/03 - 3.3.8

Application Number: 96114884.8

Publication Number: 0768379

IPC: C12N 15/12

Language of the proceedings: EN

Title of invention:
Ubiquitous potassium-channel proteins and genes for the same

Applicants:
Susumu Seino Inohana Shukusha Chiba University, et al

Opponent:
-

Headword:
Channel proteins/CHIBA UNIVERSITY

Relevant legal provisions:
EPC Art. 56

Keyword:
"Inventive step (no)"

Decisions cited:
-

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0150/03 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 25 June 2004

Appellants: Susumu Seino Inohana Shukusha Chiba et al.
University
1-103, 1-8-1, Inohana
Chuo-ku Chiba
Chiba 260 (JP)

Representative: Smart, Peter John
W.J. BECK GREENER & CO
7 Stone Buildings
Lincoln's Inn
London WC2A 3SZ (GB)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 21 August 2002 refusing European application No. 96114884.8 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: L. Galligani
Members: T. J. H. Mennessier
V. Di Cerbo

Summary of Facts and Submissions

I. The applicants (appellants) lodged an appeal against the decision of the examining division, given at oral proceedings on 11 June 2002 with written reasons posted on 21 August 2002, refusing the European patent application No. 96 114 884.8, with publication number 0 768 379, claiming priority of 18 September 1995.

II. Reasons for the refusal were lack of clarity (Article 84 EPC), lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC) of the main and the auxiliary requests then on file, claim 1 of said requests (with same wording for both) being objected only for lack of inventive step.

III. The appellants filed a statement of grounds of appeal.

IV. A communication under Article 11 of the Rules of Procedure of the Boards of Appeal presenting some preliminary and non-binding views of the board was sent to the parties.

V. In reply to the board's communication, with letter dated 21 May 2004, the appellants submitted a new main request (claims 1 to 9) to replace the requests on file, together with observations.

VI. Oral proceedings took place on 25 June 2004, where essentially the question whether the subject-matter of claim 1 involved an inventive step was discussed.

VII. Claim 1 of the main request which was identical to claim 1 of the main and the auxiliary requests refused by the examining division read:

"1. A ubiquitous, ATP-sensitive potassium-channel protein of a human origin which has the amino acid sequence shown in Fig. 1."

VIII. The following documents are cited in this decision:

(1) Nobuya Inagaki et al., J. Biol. Chem., Vol. 270, No. 11, 17 March 1995, Pages 5691 to 5694

(A) WO-A-94/19464, published on 1 September 1994

(B) WO-A-95/04820, published on 16 February 1995

IX. The appellant's arguments may be summarised as follows:

Claim 1 - Article 56 EPC

Document (1) was simply a report of a newly discovered rat protein, $uK_{atp-}1$. Whilst document (1) suggested that $uK_{atp-}1$ might have a physiological role, there was no suggestion of any practical use for the rat protein. Neither was there any indication in document (1) that a corresponding protein would exist in humans. Therefore, there would be no incentive for the skilled person to try to produce the corresponding human protein. Even if the skilled person had wished to look for the human protein, he/she would have been deterred from doing so because, firstly, document (1) stated that $uK_{atp-}1$ had not been found in the human embryonic kidney cell line HEK293, although $uK_{atp-}1$ mRNA had been found in the rat

kidney, and, secondly, there had been considerable difficulties involved in producing the human protein.

The skilled person would not have known from document (1) whether corresponding uK_{atp}-1 DNA existed in any species other than the rat. Taking a logical and stepwise approach, he/she would have not immediately attempted to find the DNA in humans, as humans were only remotely related to rats. He/she would have proceeded with looking for uK_{atp}-1 DNA in humans only if he/she had been successful in finding the DNA in species more closely related to the rat. As document (1) stated that uK_{atp}-1 had not been found in the mouse or the hamster cell lines tested, it was likely that at this stage the skilled person would have expected uK_{atp}-1 to be found only in the rat. He/she would thus never have got to the stage of looking for uK_{atp}-1 DNA in humans, and would not have made the invention.

The skilled person wishing to apply the teaching of document (1) in looking for uK_{atp}-1 in a species other than the rat would have recognised that it would not have been practical to isolate and identify the uK_{atp}-1 protein directly from the cells of said other species, but that rat uK_{atp}-1 DNA would have been needed as a probe. As the DNA sequence encoding rat uK_{atp}-1 was not reported in document (1), in order to obtain the rat uK_{atp}-1 DNA sequence, a very large number of degenerate DNA sequences would have needed to be synthesised. The sequences would then each have needed to be exposed to rat cDNA to check for hybridisation to rat uK_{atp}-1 DNA in order to determine which sequence was correct. Only then could the correct sequence have been used as a probe for cDNA in another species.

It was also clear from document (1) that rat uK_{atp}-1 DNA was similar to DNA from other potassium-channel proteins. The skilled person would have appreciated that many of the degenerate DNA sequences would have been likely to hybridise to DNA coding for potassium-channel proteins other than uK_{atp}-1 and this could have led to the isolation of DNA encoding a wrong protein.

Thus, the skilled person wishing to apply the teaching of document (1) to look for uK_{atp}-1 in a species other than the rat would have had no choice but to attempt to reproduce the method of document (1) to isolate rat uK_{atp}-1 DNA. As said method was only very briefly described, the skilled person would have been faced with a number of significant difficulties. Therefore, the expectation of success would have been very low in preparing a rat uK_{atp}-1 DNA probe, and, thus in identifying human uK_{atp}-1 DNA and finally in obtaining the human uK_{atp}-1 protein.

X. The appellants requested that the decision under appeal be set aside and that a patent be granted on the basis of claims 1 to 9 of the main request as filed on 21 May 2004.

Reasons for the Decision

Main request (sole request)

Inventive step (claim 1)

The invention

1. Claim 1 is directed to a protein of human origin having the particular primary structure represented in Figure 1. That protein which is an inward rectifier K^+ channel (see page, column 2, lines 54 to 56 in the application) is also referred to in the application as "huK$_{ATP}$-1" to distinguish it from the related protein of rat origin also referred to therein as "ruK$_{ATP}$-1".

The closest prior art and the background art

2. Document (1) is considered to represent the most appropriate starting point for the discussion of inventive step.

3. Document (1) describes the cloning and functional characterisation of a novel K$_{ATP}$ channel, designated "uK$_{ATP}$-1", which represents a new subfamily of the inward rectifier K^+ channel family. The cloning was implemented using, as a probe, a cDNA fragment encoding GIRK, a protein of another subfamily of inward rectifier K^+ channels. A rat pancreatic islet cDNA library was screened. A DNA fragment of 2389 base pairs was isolated which encoded uK$_{ATP}$-1. It was found that uK$_{ATP}$-1 mRNA was expressed in all rat tissues examined. "*Since intracellular ATP is the essential carrier of metabolic energy for **all mammalian cells***" (see

page 5694, last paragraph; emphasis added by the board), the authors made the suggestion that the protein, being expressed **ubiquitously** in normal tissue might play an important role in the regulation of K^+ permeability in almost every cell by coupling metabolic energy to the membrane potential of the cell. The document concluded with an invitation to examine how the activation and inactivation processes of uK_{ATP}-1 were regulated in altered metabolic states such as diabetes mellitus, starvation and ischemia.

4. Whereas the nucleotide sequence encoding rat uK_{ATP}-1 was not directly reported in the document, it was stated at the bottom of page 5691 that "*The nucleotide sequence(s) reported in this paper has been submitted to the GenBank™/EMBL Data Bank with accession number(s) D42145*".

5. The background art had already either indicated the existence of a **human** protein closely related (with more than 92% amino acid sequence identity) to the inward rectifier K^+-channel identified initially in the rat and known as ROMK1 (see document (A), page 12, line 24 to 26) or suggested the development of functional **human** homologues of the mouse IRK1 and rat GIRK1 inward rectifier K^+-channels (see document (B), "*Summary of the Invention*" from page 7, line 33 to page 10, line 29).

Analysis of inventive step

6. The human uK_{ATP}-1 of claim 1 and the rat uK_{ATP}-1 of document(1) differ in their primary structure (cf. Figure 1 of the application and Figure 1 of the document, respectively) only by 9 amino acids over a

total of 424 amino acids (that is a 2% amino acid sequence difference).

7. The problem solved by the invention may be regarded as the identification in human tissues of a human equivalent of the rat, a solution being represented by the protein of claim 1.

8. Whereas it is true that the teaching of document (1) focuses on a protein which is expressed in **rat** tissues, at the priority date the skilled person, who was a medical practitioner having particular interest in **human** metabolic disorders such as diabetes (in this respect, note that the work was supported by organisations interested in human diabetes research; see footnote on page 5691), would certainly have envisaged what the impact of the results presented in said document could have been on the study and treatment of human metabolic diseases such as diabetes. After all, even the last paragraph of the document contains an obvious invitation to the skilled reader to embark on a study of diabetes mellitus, starvation and ischemia which are diseases affecting the human beings.

9. In the board's judgment, the fact that uK_{ATP}-1 was not found to be expressed in a culture of a particular human cell line, namely the embryonic kidney cell line HEK293, would not have led the skilled reader to the idea that said protein or a homolog thereto could not be found in human tissues, ie to a sort of prejudice against finding it in humans. The skilled person would have noted in fact that the protein had not been found to be expressed in a number of other cell lines whatever their origin (see the paragraph bridging

pages 5693 and 5694 in document (1)) and would therefore have considered this to be a peculiarity of those cell lines. Moreover, the reference to "***all mammalian*** *cells*" in the last paragraph on page 5694 of document (1) was an obvious indication that the authors of the document did not intend to confine their further investigations to the rat but on the contrary to extend them to other mammals, more particularly to the human beings as supported by the further reference also made on the same page 5694 to a disease such as diabetes mellitus which primarily concerns humans.

10. From the state of the art (see point 5, supra), the person skilled of the art would have known that the identification of human homologs of inward rectifier K^+-channels initially found in the rat or the mouse was a field of active investigation at the priority date.

11. Moreover, using the GenBank™/EMBL accession number D42145 referred to in document (1) (see point 4, supra), the skilled person would have been in a position to retrieve directly all the necessary information about the nucleotide sequence encoding the rat uK_{ATP}-1, useful for easily preparing therefrom a cDNA fragment to be used as a probe to screen a human cDNA library and to identify a cDNA encoding a human homolog of the ruK_{ATP}-1.

12. In view of the above analysis, the board concludes that the skilled person would have regarded the teaching of document (1) as a strong incentive to look for a human homolog of the rat uK_{ATP}-1 and that he/she would have arrived with a reasonable expectation of success at the solution proposed in claim 1, ie at the protein the

primary structure of which is depicted in Figure 1 of the application.

Conclusion

13. Therefore, the board comes to the conclusion that claim 1 does not involve an inventive step, and, thus, that the sole request on file is not allowable under Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed

The Registrar: The Chairman:

W. Wolinski L. Galligani