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Datasheet for the decision of 22 June 2006

Case Number: T 1439/04 - 3.3.08

Application Number: 96935546.0

Publication Number: 0863203

IPC: C12N 15/10

Language of the proceedings: EN

Title of invention:
Method for expression cloning of gene encoding protein kinase substrate protein

Applicant:
Tanaka, Toshio

Opponent:
-

Headword:
Kinase substrate protein/TANAKA

Relevant legal provisions:
EPC Art. 56, 113(1)

Keyword:
"Main and auxiliary requests - inventive step (no)"

Decisions cited:
-

Catchword:
-

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Case Number: T 1439/04 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 22 June 2006

Appellant: Tanaka, Toshio
2673-2, Fujikata
Tsu-shi
Mie 514 (JP)

Representative: Geering, Keith Edwin
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 13 August 2004 refusing European application No. 96935546.0 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: F. Davison-Brunel
Members: M. R. Vega Laso
C. Rennie-Smith

Summary of Facts and Submissions

I. The applicant (appellant) lodged an appeal against the decision of the examining division posted on 13 August 2004, whereby the European patent application No. 96 935 546.0 was refused pursuant to Article 97(1) EPC. The European application was filed as international application PCT/JP96/03234 and published in an official language as EP 0 863 203 A1. The refusal was based on the finding that the subject-matter of the claims then on file did not involve an inventive step within the meaning of Article 56 EPC.

II. In the statement setting out the grounds of appeal, the appellant maintained the claim request on the basis of which the application had been refused as his main request. Additionally, an auxiliary claim request (claims 1 to 9) was filed with the statement. The appellant requested oral proceedings under Article 116 EPC, in case the board did not intend to allow either of his requests.

III. The examining division did not rectify its decision and, pursuant to Article 109(2) EPC, remitted the appeal to the boards of appeal.

IV. The appellant was summoned to oral proceedings. In a communication under Article 11(1) of the Rules of Procedure of the Boards of Appeal ("RPBA") sent with the summons, the board expressed its provisional opinion on some of the issues to be discussed during the oral proceedings.

V. In his reply to the board's communication, the appellant withdrew the main request then on file and indicated that the auxiliary claim request filed with the statement of grounds of appeal became his main request.

VI. Claim 1 of the **main request** read:

"1. An expression cloning method of a gene coding for a protein kinase substrate protein having a self-phosphorylating ability comprising the steps of:

plate-culturing a host into which DNA inserted into an expression vector has been introduced wherein said DNA has been cloned from normal cell(s) or tissue or from cell(s) or tissue in a disease state,

expressing said DNA,

transferring protein produced from the plate to a film contacting the film with the plate,

removing said film from said plate,

adding a phosphate donor to said film to phosphorylate said protein,

detecting phosphoric acid bonded to said protein, and

isolating DNA from the host clones on the plate corresponding to the sites on the film that exhibit a positive reaction."

Claims 2 to 9 concerned different embodiments of the cloning method of claim 1.

VII. In a second communication in preparation for the oral proceedings, the board expressed its provisional view on the issue of inventive step with regard to the claim

request on file, as well as observations on a possible amendment to the claims.

VIII. On 16 June 2006, the appellant replied to the board's communication and submitted a new **auxiliary request** (claims 1 to 7). This request differed from the main request on file in that the sentence "*...; wherein protein kinase is not added in the method.*" had been inserted at the end of claim 1, and claims 8 and 9 had been deleted. The appellant also informed the board of his intention not to attend the scheduled oral proceedings.

IX. Oral proceedings were held on 22 June 2006 in the absence of the appellant.

X. The following documents are cited in the present decision:

(1): G. Carmel and J. Kuret, Analytical Biochemistry, 1992, Vol. 203, pages 274 to 280;

(2): F. Valtorta et al., Analytical Biochemistry, 1986, Vol. 158, pages 130 to 137.

XI. The arguments put forward by the appellant in writing may be summarised as follows:

Main request

Document (1) taught only phosphorylation in the presence of a (cAMP-dependent) protein kinase. It could not, therefore, suggest the claimed method which related to proteins having self-phosphorylating

activity and which did not require protein kinase. The point was not whether the skilled person could have arrived at the invention by modifying the prior art, but rather whether, in expectation of the advantages achieved, he/she would have done so because of promptings in the prior art. There was no prompting in document (1) towards a method of expression cloning a gene coding for a protein kinase substrate protein having a self-phosphorylating ability, and hence there could have been no expectation of the advantages achieved.

Document (1) was published over 3.5 years before the priority date of the invention. If the invention had been a "normal design variant", as alleged by the examining division, the interval between the publication of document (1) and the priority date of the invention would have been rather shorter. The lengthy interval was further evidence of an inventive step.

Auxiliary request

Document (2) taught only that the presence of proteins with self-phosphorylating ability was disadvantageous. The last paragraph of the right column, page 136 concerned limitations of the solid-phase phosphorylation assay caused by proteins with self-phosphorylating activity, and did not suggest or advocate the specific and/or advantageous application of the described phosphorylation assay to such proteins. Indeed, document (2) taught away from this type of proteins, indicating how the problems caused by their presence (high background noise) could be solved or

circumvented. In the absence of any promptings in document (2), the allegation of obviousness was only possible with the benefit of the impermissible use of hindsight.

XII. The appellant requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed with the statement of grounds of appeal as the auxiliary request or on the basis of the new auxiliary request filed on 16 June 2006.

Reasons for the Decision

1. The issue to be decided in this appeal is whether or not the subject-matter of either the main request or the auxiliary request involves an inventive step.

Main request

2. Document (1) is considered to be the closest prior art. This document is concerned with finding out the consensus recognition sequence for a protein kinase in a substrate protein. It proposes a method in which oligonucleotides designed as a cassette comprising a codon for a phosphorylatable serine residue flanked on both sides by codons for various amino acids, are inserted into a gene encoding a modified BCY1 protein (BCY1Δ protein). The resulting recombinant BCY1Δ genes, each having a different cassette, are then inserted into expression vectors, and the recombinant DNAs thus obtained are transformed into host cells. Clones that express a BCY1Δ protein containing a phosphorylation

site are screened for by probing with a protein kinase and a phosphate donor in a solid-phase phosphorylation assay. As a control, host cells carrying an expression vector comprising an intact BCY1 gene are also tested in the assay.

3. In the light of the disclosure of document (1), the technical problem to be solved is defined as developing an expression cloning method for further protein kinase substrate proteins. The simple formulation of this problem cannot be considered to contribute to an inventive step, because furthering the existing state of knowledge belongs to the routine tasks with which the skilled person is forever occupied.

4. The solution proposed in claim 1 is a method for cloning a gene which encodes a protein kinase substrate protein having a self-phosphorylating ability, which method comprises the same steps as the method described in document (1). It should be noted that in the screening step of the method of claim 1 probing with a phosphate donor is explicitly required, but the use of a protein kinase is not excluded. Hence, in the light of claim 1 the technical contribution of the alleged invention to the art may be defined as the application of a known expression cloning method for genes encoding protein kinase substrate proteins to the cloning of a particular type of protein kinase substrate proteins, namely substrate proteins having a self-phosphorylating ability.

5. In the present case, the relevant question in relation to inventive step is whether or not, in view of the disclosure of document (1) supplemented with the common

general knowledge of the person skilled in the art at the priority date, it was obvious to try to clone protein kinase substrate proteins having a self-phosphorylating ability using the method disclosed in document (1), and whether there was a reasonable expectation of success.

6. It has not been disputed by the appellant that, at the priority date, it was part of the common general knowledge of the skilled person that, whereas some protein kinase substrate proteins having a phosphorylatable site are phosphorylated by a separate kinase protein, there also exist protein kinase substrate proteins which are capable of self-phosphorylation, the transfer of a phosphate molecule from the phosphate donor to the phosphorylatable site of the substrate protein being catalyzed by the protein itself.

7. A skilled person reading document (1) could readily recognise that the screening method described in this document relies on the presence of a phosphorylatable site of the substrate protein. Since the skilled person knew that substrate proteins having self-phosphorylating ability present phosphorylatable sites, it did not require any inventive skills to conclude that the screening method described in document (1) would also identify substrate proteins capable of self-phosphorylation. Consequently, even though document (1) does not mention self-phosphorylating proteins, let alone suggests that the cloning method disclosed therein may be applied to such proteins, the board considers that, having regard to the teaching of this document supplemented with the common general knowledge

at the priority date, it was obvious to apply the method of document (1) to the cloning of genes that encode self-phosphorylating proteins.

8. Neither objective difficulties nor a prejudice that would prevent the skilled person from trying to clone such genes using the method disclosed in document (1) have been alleged, and the board is unable to see any. Furthermore, in the absence of a documented technical prejudice, the board cannot consider a time interval of 3.5 years between the publication of document (1) and the priority date of the application to be an indication of inventive skills being required to arrive at the claimed method.

9. Consequently, the subject-matter of claim 1 of the main request is considered to lack an inventive step within the meaning of Article 56 EPC.

Auxiliary request

10. The solution proposed in claim 1 is a method comprising the same steps as the method described in document (1), except for the fact that no protein kinase is added.

11. The technical problem to be solved may be defined as providing an expression cloning method specific for genes encoding substrate proteins having self-phosphorylating ability.

12. Document (2), to which document (1) refers in connection with the solid-phase phosphorylation assay used to screen an expression library (cf. page 275, left column, line 7), teaches that when the

phosphorylation assay is carried out in the presence of a phosphate donor and a protein kinase, both substrate proteins for the used protein kinase and self-phosphorylating proteins are identified (cf. page 136, right column, second sentence of the last paragraph). Since the phosphorylation assay was intended for identifying substrate proteins phosphorylated by a specific kinase, the concurrent detection of self-phosphorylating substrate proteins was considered disadvantageous. Accordingly, the authors suggested two ways to circumvent this problem (cf. paragraph bridging pages 136 and 137).

13. Admittedly, document (2) does not suggest omitting the kinase in the phosphorylation assay. However, in the light of this passage it was obvious to a person skilled in the art, who may be defined as a biochemist specialized in the field of protein kinases confronted with the problem of cloning **specifically** substrate proteins with self-phosphorylating ability, not only that a modification of the screening method known from the prior art is necessary, but also which modification is necessary in order to prevent substrate proteins other than those having self-phosphorylating ability from being phosphorylated, namely to omit the protein kinase from the assay. In the board's view, neither were inventive skills necessary for arriving at this solution nor were any difficulties to be expected.

14. Accordingly, the solution proposed by claim 1 is obvious and, consequently, the auxiliary request does not fulfil the requirement of Article 56 EPC.

Article 113(1) EPC

15. In his letter dated 16 June 2006, the appellant stated that "it would seem appropriate for the proceedings to be continued in writing". The board disagrees with this view. From a substantive point of view, there is no further request on file on the basis of which examination of the application could be continued. From the procedural point of view, it should be noted that the reasons given by the board in the present decision were apparent from the communications sent in preparation for the oral proceedings. The appellant was given the opportunity to put forward its counter-arguments both in writing and during oral proceedings; he chose, however, not to attend the oral proceedings to which he had been duly summoned. Pursuant to Rule 71(2) EPC, oral proceedings were held in the appellant's absence (see also Article 11(3) RPBA). In view of the above, the board is satisfied that the provisions of Article 113(1) EPC have been complied with.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

G. Nachtigall F. Davison-Brunel