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Datasheet for the decision of 12 May 2011

Case Number: T 0076/09 - 3.3.08

Application Number: 01983266.6

Publication Number: 1305627

IPC: G01N 33/531

Language of the proceedings: EN

Title of invention:
Protein fragment complementation assay based on beta-lactamase

Applicant:
Odyssey Thera, Inc.

Opponent:
-

Headword:
Protein fragment complementation assay/ODYSSEY

Relevant legal provisions:
EPC Art. 83, 84, 111(1), 123(2)

Relevant legal provisions (EPC 1973):
-

Keyword:
"New main request - Requirements of Articles 123(2), 84 and 83 (met)"

Decisions cited:
G 0001/03

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0076/09 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 12 May 2011

Appellant: (Applicant)
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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 5 August 2008 refusing European patent application No. 01983266.6 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman: M. Wieser
Members: M. R. Vega Laso
J. Geschwind

Summary of Facts and Submissions

I. The appeal of the applicant (appellant) lies from the decision of the examining division of the European Patent Office posted on 5 August 2008, by which European Patent Application No. 01 983 266.6 with the title "Protein fragment complementation assay based on beta-lactamase", filed as PCT/US01/17886 on 1 June 2001 and published as WO01/94617, was refused pursuant to Article 97(2) EPC on the grounds that the set of claims then on file offended against Article 123(2) EPC and did not conform to Article 84 EPC.

II. In particular, the examining division found that there was no basis in the application as filed for either the particular fragments of the TEM-1 ß-lactamase (amino acid residues 24 to 194 and amino acid residues 196 to 286), or the particular point mutations (E102K, M180T, G236S) specified in claims 1, 28, 34 and 35 as then on file. Moreover, the examining division refused to allow a correction of the application under Rule 139 EPC in order to adapt it to the amended claims, on the grounds that it was not immediately evident to a person skilled in the art that nothing else would have been intended than what was offered as correction (see points 1 to 5 of the Reasons in the decision under appeal).

III. Together with its statement of grounds of appeal, the appellant re-filed as its main request the set of claims on the basis of which the application was refused. Two additional sets of claims were filed as first and second auxiliary request, respectively. As a subsidiary request, oral proceedings under Article 116 EPC were requested.

IV. The examining division did not rectify its decision and the appeal was remitted to the boards of appeal (Article 109 EPC).

V. The appellant was summoned to oral proceedings. In a communication under Rule 15(1) of the Rules of Procedure of the Boards of Appeal attached to the summons, the board expressed its provisional opinion on some of the issues to be discussed at oral proceedings.

VI. In reply to the communication, the appellant submitted a set of amended claims which replaced the previous claims according to its main request.

VII. Oral proceedings were held on 12 May 2011. During the oral proceedings, a set of amended claims (claims 1 to 4) was filed as fresh main request.

VIII. Independent claim 1 of the new main request reads:

"1. An in-vivo protein complementation assay (PCA) method for detecting protein-protein interactions in mammalian host cells comprising:

(A) expressing within the host cells at least:

(i) a first recombinant polypeptide which comprises a first interacting domain linked to a first fragment of a ß-lactamase reporter molecule by a flexible linker, and

(ii) a second recombinant polypeptide which comprises a second interacting domain linked to a second fragment of said ß-lactamase reporter molecule by a flexible linker;

(B) allowing interaction of the interacting domains; and

(C) detecting reconstituted reporter molecule activity within the host cells;

wherein an esterified derivative of nitrocefin is used as substrate of said reporter molecule, with the proviso that said method is not practised on the human or animal body."

Dependent claims 2 to 4 concern particular embodiments of the method of claim 1.

IX. The arguments put forward by the appellant, as far as they are relevant to this decision, may be summarized as follows:

Article 123(2) EPC

An assay method for the detection of "*protein-protein interactions*" was disclosed in the passage on page 1, lines 8 and 9 of the application as filed. The feature "*an esterified derivative of nitrocefin is used as substrate of said reporter molecule*" had a basis in the passage on page 7, line 21 in connection with page 8, lines 1 to 3 of the application as filed. The wording "*a flexible peptide linker*" was included in claim 24 in the context of claims 18 and 19 of the original patent application. The feature "*with the proviso ...*" was introduced in order to overcome an objection of the examining division under Article 52(4) EPC 1973.

Article 84 EPC

In the context of the application (see page 8, lines 4 and 10), the wording "in-vivo" meant that intact cells were used for the assay.

X. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of claims 1 to 4 of the new main request filed during the oral proceedings.

Reasons for the Decision

Main request - Article 123(2) EPC

1. Amended claim 1 of the main request is derived from the corresponding claim of the application as filed, which has been amended to delete the wording of the second alternative in step (A), and to introduce additional features disclosed in the description and/or the claims of the original application as well as a negative feature (disclaimer).

2. The assay method of present claim 1 is defined as a protein complementation assay (PCA) for detecting protein-protein interactions. This feature can be derived from the passage on page 1, lines 6 to 9 of the application as filed which concerns the technical field of the invention. The use of mammalian cells as host cells is disclosed in the passage on page 1, lines 15 to 21 of the application as filed.

3. As regards the feature "*in-vivo*" characterising the claimed assay method, it is stated in the passage bridging pages 7 and 8 of the application as filed that:

> "*... this assay, at present is performed with whole cell lysates, as nitrocefin is not membrane permeant. However, in principle addition of ester groups could be sufficient to allow for membrane permeability and a true* ***in vivo*** *colorimetric assay could be performed*"
> (see line 28 on page 7 and lines 1 to 3 on page 8 of the application as filed; emphasis added by the board)

In the board's judgement, this passage provides an adequate basis for an in-vivo assay method in which an esterified derivative of nitrocefin is used as substrate.

4. Like the assay method of claim 1 of the application as filed, the method according to present claim 1 comprises three steps (steps (A) to (C)). In step (A), a first and second recombinant polypeptide is expressed in the host cells. While in present claim 1 the wording "*expressing*" is used instead of "*generating*" as in the corresponding claim of the application as filed, in the board's view, a person skilled in the art understands immediately from the content of the application as a whole that the recombinant polypeptides can be generated by providing nucleic acid molecules which code for the polypeptides "*and subsequently allowing said nucleic acid molecules to produce their coded products*" (see alternative 2 in step (A) of claim 1 of the application as filed). It is also apparent from the

examples in the application as filed that, in an embodiment of the disclosed protein complementation assay method, the host cells used for the assay have been transfected with an eukaryotic expression vector (pMT3) which includes constructs encoding the recombinant polypeptides (see Example 3 on page 10 of the application as filed, in particular lines 5 and 6, and Example 1).

5. As concerns the features introduced to characterise the first and second recombinant polypeptides, a basis is found in claims 19, 21 and 24 of the application as filed. Claim 19 of the application as filed provides a general disclosure of a first/second compound comprising a first/second fragment of an interacting domain linked to a first/second fragment of a reporter molecule. In claim 21 of the application as filed, the reporter molecule is characterized as a ß-lactamase, and in claim 24 it is specified that at least one of the compounds has a flexible linker joining its reporter molecule fragment to its associated interacting domain.

6. Steps (B) and (C) of the assay method of present claim 1 are identical to those in the method of claim 1 of the application as filed, except for the feature "*within the host cells*" introduced in step (C), which can be derived from the disclosure of an "*in-vivo*" assay method (see paragraph 3 above and paragraph 10 below).

7. The negative feature "*with the proviso that said method is not practised on the human or animal body*" included in claim 1 was introduced by the applicant - the

present appellant - in response to an objection of the examining division under Article 52(4) EPC 1973. The feature in question excises from the scope of the claim subject-matter which is excluded from patentability for non-technical reasons, and thus fulfils a criterion established by the Enlarged Board of Appeal for a disclaimer which is not disclosed in the application as filed to be considered allowable under Article 123(2) EPC (see decision G 1/03 (OJ EPO 2004, 413; Headnote point 2.1, third paragraph).

8. The additional feature characterising the method of dependent claim 2 specifies that the mammalian host cells are transfected with nucleic acid molecules which encode the first recombinant polypeptide and the second recombinant polypeptide. This feature is derivable from the examples of the application as filed, in particular Example 3 in connection with Example 1 (see paragraph 3 above). Claims 3 and 4 have a basis in claims 22 and 23 of the application as filed.

9. In view of the above, the board is convinced that the amendments introduced into the set of claims according to the main request conform to Article 123(2) EPC.

Article 84 EPC

10. At the oral proceedings before the board, the clarity requirement of Article 84 EPC was discussed with regard to the feature "*in-vivo*" characterising the assay method of claim 1. In the board's judgement, in view of the disclosure in the present application as a whole, the wording "*in-vivo*" must be interpreted as opposed to the term "*in vitro*", which in the context of the assays

disclosed in the application as filed means "in a cell lysate" (see, *inter alia*, Example 4 in the application). Thus, an "in-vivo" PCA assay method within the meaning of claim 1 is understood as an assay method carried out using whole (i.e. not lysed), living host cells.

11. The objections under Article 84 raised by the examining division in the decision under appeal (see paragraphs 6.1 and 6.2 of the decision) are not pertinent to the claims as presently on file, which are considered to meet the requirements of Article 84 EPC.

Article 83 EPC

12. The comments made by the examining division in point 6 of its decision do not apply to the present claims. Since there is no evidence on file showing that the claimed assay method could not be carried by a person skilled in the art using the technical information provided in the application supplemented by its own common general knowledge, the requirement of Article 83 EPC is regarded as fulfilled.

Remittal to the department of first instance

13. In the decision under appeal, only issues under Article 123(2), 84 and 83 were considered by the examining division. The board, after having ascertained that the requirements of these articles of the EPC are met by the claims of the main request, exercises its discretion under Article 111(1) EPC and remits the case to the department of first instance for further prosecution.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution on the basis of the claims 1 to 4 of the new main request filed during the oral proceedings.

The Registrar: The Chairman:

A. Wolinski M. Wieser