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Datasheet for the decision of 13 January 2011

Case Number: T 0786/08 - 3.3.04

Application Number: 98918819.8

Publication Number: 1017710

IPC: C07K 5/00

Language of the proceedings: EN

Title of invention:
Inhibitors of the JNK signal transduction pathway and methods of use

Applicant:
University of Massachusetts

Opponent:
-

Headword:
Inhibitors of JNK/UNIVERSITY OF MASSACHUSETTS

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

Relevant legal provisions (EPC 1973):
-

Keyword:
"New Main Request: added subject-matter (no)"
"Sufficiency of disclosure (yes)"
"Clarity (yes)"

Decisions cited:
-

Catchword:
-

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Case Number: T 0786/08 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 13 January 2011

Appellant: (Applicant)
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 30 November 2007 refusing European application No. 98918819.8 pursuant to Article 97(1) EPC 1973.**

Composition of the Board:

Chairman: C. Rennie-Smith
Members: R. Gramaglia
G. Alt

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division, whereby European patent application No. 98 918 819.8, published as WO-A-98/49188, was refused pursuant to Article 97(1) EPC 1973. The reason given by the examining division for refusal was that the claims of the sole request then on file did not fulfil the requirements of Articles 123(2), 83 and 84 EPC.

II. With a Statement of Grounds of Appeal filed on 31 March 2008, the appellant submitted a Main Request, identical to that refused by the examining division, and a First Auxiliary request.

III. In a communication annexed to the summons to oral proceedings, the board provided its preliminary opinion, expressing doubt, inter alia, about whether claim 7 fulfilled the requirements of Article 84 EPC.

IV. In response thereto, the appellant submitted with the letter dated 4 November 2010 a New Main Request, differing from the previous Main Request only in that claims 7 and 15 had been deleted and the remaining claims accordingly renumbered.

V. Claim 1 of this request read as follows:

"1. A c-Jun NH2 terminal kinase (JNK)-interacting protein 1 (JIP-1) polypeptide, said polypeptide comprising SEQ ID NO:1, or SEQ ID NO:1 with at least one conservative amino acid substitution, wherein the polypeptide specifically inhibits the activity of JNK".

Claims 2 to 6 related to specific embodiments of the polypeptide of claim 1. Claims 7 to 10 and 13 related to nucleic acids encoding the polypeptide of claim 1. Claims 11 and 12 were directed to a host cell and an expression vector, respectively, comprising the nucleic acid of claim 7. Claims 14 to 18 addressed medical uses of the polypeptide of claim 1.

VI. Oral proceedings were held on 13 January 2011.

VII. The submissions by the appellant (applicant), insofar as they are relevant to the present decision, can be summarized as follows:

Article 123(2) EPC

– There was a basis for the wording "with at least one conservative amino acid substitution" in claims 1, 2 5 and 9 on page 4, line 34 to page 5, line 4 of the published WO application, when read in the light of the passage on page 2, line 28 to page 3, line 22 and Example 11.

Article 83 EPC

– The patent application provided the information necessary for engineering the claimed conservative amino acid substitutions that preserved the JIP-1 capacity to inhibit JNK activity.

Article 84 EPC

– There was an explanation of the term "conservative amino acid substitution" on page 12, lines 7-14 of the published WO application.

VIII. The appellant requested that the decision under appeal be set aside and that the case be remitted to the department of first instance for further prosecution on the basis of the claims of the New Main Request filed with its letter of 4 November 2010.

Reasons for the Decision

Article 123(2) EPC

1. Present claim 1 is based on the combination of claims 1 and 5 as filed with the passage on page 2, lines 33-34 of the published WO application, relating to the biological activity. Further, the wording "substantially identical" in original claim 5 has been replaced with the expression "with at least one conservative amino acid substitution".

2. The examining division (see paragraph 1 of the decision under appeal) came to the conclusion that the wording "with at least one conservative amino acid substitution" had no basis in the following passage of the published WO application (see page 4, line 34 to page 5, line 4):

"A substantially identical polypeptide sequence differs from a given sequence only by conservative amino acid

substitutions or by one or more nonconservative substitutions, deletions, or insertions located at positions which do not destroy the function of the polypeptide compared to wild-type JIP-1".

3. The examining division noted that present claim 1 no longer comprised the term "only" (in bold and underlined in paragraph 1 of the decision under appeal), which was present on page 4, line 35 of the published WO application, and concluded that the expression in claim 1 "with at least one conservative amino acid substitution" went beyond the application as filed because it did not exclude "additional modifications" other than conservative amino acid substitutions, unlike the original wording.

4. It should be established whether or not the expression in claim 1 "with at least one conservative amino acid substitution" goes beyond the application as filed. The board observes that the passage on page 4, line 34 to page 5, line 4 of the original WO application (see point 2 supra) relates to two different options linked by the term "or" (exclusive), namely (i) a polypeptide is "substantially identical" to the given polypeptide if it differs from a given sequence only by conservative amino acid substitutions **or** (ii) a polypeptide is "substantially identical" to the given polypeptide if it differs from a given sequence only by nonconservative amino acid substitutions, deletions or insertions. Therefore, it cannot be derived from this passage (with or without the term "only" on page 4, line 35) that a polypeptide is "substantially identical" to the given polypeptide if it differs from a given sequence by a combination of conservative **and**

nonconservative amino acid substitutions, deletions or insertions.

5. It follows that the board neither sees that the selection of option (i) (see point 4 supra), with the omission of "only", resulting in the expression in present claim 1 "with at least one conservative amino acid substitution", goes beyond the application as filed, nor that claim 1 relates (as the examining division suggested - see point 3 supra) to "additional modifications" other than conservative amino acid substitutions.

6. Therefore, the subject-matter of claim 1 does not go beyond the content of the application as filed. This conclusion extends to claims 2, 5 and 9, comprising all the wording "with at least one conservative amino acid substitution".

Article 83 EPC

7. In paragraph 2 of the decision under appeal, the examining division found that claim 1 contravened Article 83 EPC because it encompassed polypeptides having an unlimited number of amino acid substitutions (i.e. polypeptides having up to 0% sequence identity with SEQ ID NO:1) and that the present application did not teach how to generate a polypeptide corresponding to SEQ ID NO:1 with all positions mutated and retaining the ability to inhibit specifically the activity of JNK.

8. However, in the board's judgment, the application provides the technical information as to how to obtain JIP-1 variants following the genetic engineering route

(see page 14, line 1 to page 20, line 2) or by chemical synthesis (see page 20, lines 3-7). Example 10 describes the screening for polypeptides with JIP-1 activity. Therefore, the skilled person would at the priority date of the application have been in a position to arrive by routine methods at mutants differing from SEQ ID NO:1 referred to in claim 1 and would have been able to test these mutants for inhibition of JNK activity, and to select those which had such biological activity. There is thus no evidence before the board that the skilled person could not find, without undue burden, many variants of SEQ ID NO:1 which both have one or more conservative amino acid substitutions and specifically inhibit the activity of JNK.

9. Moreover, it appears unreasonable to assume, as the examining division apparently did, that the skilled person (a protein chemist) would expect that JIP-1-analogs devoid of amino acid homology to JIP-1, especially in the substantial part of the polypeptide being the active centre (the JNK-binding domain referred to on page 11, lines 9-11), or in the conserved amino acid positions (some of which are referred to on page 13, line 29), as if all the 660 amino acids of JIP-1 were replaced by Gly, or Ala, would lead to an active protein.

10. Thus, the situation here, where the claimed products are limited to those having a certain physical relation to one another and to JIP-1, and a testable narrowly defined activity, must be distinguished from situations where the structure and/or the activity is/are not defined in a disputed claim, so that it can be said

that some molecules fall within the claim, but the description gives no guidance as to how they can be made and/or successively tested.

11. In summary, the board cannot, in these circumstances, see any grounds for saying that the subject-matter of claim 1 is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. This conclusion also applies, mutatis mutandis, to claims 7 to 10 and 13, relating to nucleic acids encoding the polypeptide of claim 1.

Article 84 EPC

12. As regards this Article, the examining division maintained that the term "conservative amino acid substitution" in claims 1, 2, 5 and 9 was unclear because there were several ways to define "conservative amino acids", leading to ambiguity. It was argued that groups of conservative amino acids could be based on common chemical properties, as suggested in the present application on page 12, lines 2 to 14 and lines 28 to 31 or based on a matrix obtained from the analysis of substitutions observed in homologous proteins (alignment programs usually determine if a substitution is conservative using such matrices).

13. However, as admitted by the examining division, the analysis of a matrix for comparing the substitutions observed in homologous proteins serves for establishing whether or not an amino acid position is conserved or not. But the concept of "conserved position" (as opposed to "variable position") (see page 12, line 26) bears no relationship to (and should not be confused

with) that of "conservative amino acid substitution" (as defined on page 12, lines 1 to 14 as a "mild" amino acid substitution), which is thus clear.

14. The board is thus satisfied that the claims of the New Main Request satisfy the requirements of Articles 123(2), 83 and 84 EPC.

Remittal

15. The reasons for refusing the patent application by the examining division do not apply to the claims of the present request. As the substantive issues of novelty and inventive step have not yet been the subject of discussion, the board, exercising its discretion under Article 114(1) EPC, remits the case to the examining division 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 of the New Main Request filed with the letter of 4 November 2010.

The Registrar: The Chairman:

P. Cremona C. Rennie-Smith