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Datasheet for the decision of 10 June 2020

Case Number: T 1095/17 - 3.3.04

Application Number: 08020752.5

Publication Number: 2062918

IPC: C07K16/40, C12N9/06, C12N15/53, A61P35/00, G01N33/574, C12Q1/68

Language of the proceedings: EN

Title of invention:
Pharmaceutical compositions and methods useful for modulating angiogenesis, inhibiting metastasis and tumor fibrosis, and assessing the malignancy of colon cancer tumors

Applicant:
Technion Research & Development Foundation Ltd.

Headword:
Anti-LOR-1 antibody for use in treating fibrosis/TECHNION

Relevant legal provisions:
EPC Art. 56

Keyword:
Main (sole) request - inventive step (no)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
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Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1095/17 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 10 June 2020

Appellant: (Applicant)	Technion Research & Development Foundation Ltd. Senate House Technion City 32000 Haifa (IL)
Representative:	Goodfellow, Hugh Robin Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 25 November 2016 refusing European patent application No. 08020752.5 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chair	P. de Heij
Members:	R. Morawetz
	B. Rutz

Summary of Facts and Submissions

I. The applicant's (appellant's) appeal lies from the examining division's decision refusing European patent application No. 08 020 752.5 (application as filed). The application is a divisional application of European patent application No. 03 777 136.7, having a filing date of 27 November 2003 and claiming a priority date of 27 November 2002.

II. In the decision under appeal, the examining division held that the invention to which the set of claims filed with the appellant's letter dated 25 June 2015 (sole claim request) related was insufficiently disclosed (Article 83 EPC).

III. With the statement of grounds of appeal, the appellant maintained the set of claims underlying the decision under appeal as their sole claim request and provided arguments with respect to the requirements of Article 83 EPC.

Claim 1 of the sole claim request reads:

"1. A molecule capable of downregulating a tissue level and/or activity of at least one type of lysyl oxidase for use in treating fibrosis in a mammal, wherein said molecule is an antibody or an antibody fragment directed against at least an antigenic portion of a polypeptide of SEQ ID NO: 2."

IV. The following documents are referred to in this decision:

D3 Kagan H. M., Acta Tropica (2000), vol. 77, pages 147 to 152

D12 WO 02/11667 (14 February 2002)

V. The board arranged oral proceedings as requested by the appellant, and issued a communication pursuant to Article 15(1) RPBA. The board introduced document D12, which was cited in the European search report drawn up for the present application, into the appeal proceedings (see points 6 and 15 to 17 of the board's communication). The board further indicated that it considered document D3 to be the closest prior art and that obviousness of the claimed solution over the combined teachings of documents D3 and D12 was an issue to be discussed at the oral proceedings (see points 18 to 21 of the board's communication).

VI. In response, the appellant informed the board that they would not attend the oral proceedings.

VII. Oral proceedings took place as scheduled. At the end, the chair announced the board's decision.

VIII. The appellant's arguments submitted in writing and as far as relevant to the present decision are summarised as follows:

Methods to raise antibodies against a known target were part of common general knowledge. The specific target of the antibody had been fully defined as the polypeptide of SEQ ID NO: 2. Lysyl oxidase activity was readily testable in an assay and the skilled person

seeking to reproduce the invention had to produce monoclonal antibodies (by routine methods) and test them in an assay to select the inhibitory antibodies. The data set forth in the application as filed met the standard for supporting a therapeutic indication because the application disclosed *inter alia* that LOR-1 was specifically expressed in endothelial cells of blood vessels, unlike other lysyl oxidases, and high levels of LOR-1 were observed specifically in fibrotic tissues.

IX. The appellant requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the set of claims filed with letter dated 25 June 2015.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is therefore admissible.

2. The duly-summoned appellant was neither present nor represented at the oral proceedings. The board continued the proceedings in the appellant's absence in accordance with Rule 115(2) EPC. The appellant was treated as relying on their written case in accordance with Article 15(3) RPBA.

Sufficiency of disclosure (Article 83 EPC) - claim 1

3. One embodiment falling within the scope of claim 1 is a molecule capable of downregulating the activity of at least one type of lysyl oxidase for use in treating fibrosis, wherein said molecule is an antibody directed against at least an antigenic portion of LOR-1, a lysyl oxidase having the amino acid sequence depicted in

SEQ ID NO: 2.

4. The board agrees with the appellant that the target of the antibody has been defined by indicating the amino acid sequence of LOR-1 (SEQ ID NO: 2), that raising antibodies against a known target is part of common general knowledge, and that lysyl oxidase activity is readily testable in an assay.

5. The application discloses that LOR-1 is specifically expressed in endothelial cells of blood vessels, unlike other lysyl oxidases (see page 49, lines 24-26), and that high levels of LOR-1 are observed specifically in fibrotic liver tissues (see page 50, lines 25-29).

6. Document D3, a review article, illustrates the knowledge of the skilled person with respect to the role of lysyl oxidases in fibrosis and the control of fibrosis at the priority date of the present application. Thus it was known that fibrosis is characterised by the excess accumulation of essentially insoluble collagen fibres (see page 147, left-hand column, lines 1 to 2) and that lysyl oxidase is the enzyme which initiates covalent crosslinking of extracellular collagen molecules, converting them into insoluble fibres (see page 148, right-hand column, second paragraph). Lysyl oxidase expression is markedly elevated in several instances and models of fibrotic disease, and chemotherapeutic inhibition may prove useful for the control of fibrosis (see page 149, right-hand column, second paragraph). Active site-directed lysyl oxidase inhibitors are known, β-aminopropionitrile (BAPN) being the best known (see page 150, right-hand column, second paragraph). Several studies reported the application of BAPN as an antifibrotic agent in models of fibrotic disease, and

observed beneficial, fibrosis-suppressing effects of BAPN in models of lung fibrosis (see page 150, right-hand column, third paragraph).

7. The board concludes that, in the light of the skilled person's common general knowledge, the data set forth in the application as filed meet the standard for supporting a therapeutic indication of the inhibitory antibodies in treating fibrosis.

8. Therefore the board is satisfied that the application as filed provides the skilled person, in the light of their common general knowledge, with all the information necessary for carrying out the claimed invention, as regards the provision of an antibody capable of downregulating the activity of at least one type of lysyl oxidase and its use in treating fibrosis, without undue burden.

Inventive step (Article 56 EPC) - claim 1

Closest prior art

9. Document D3 can be taken to represent the closest prior art for the claimed invention. Its teaching has been summarised in point 6. above.

Objective technical problem

10. The difference between the teaching of document D3 and the embodiment under consideration (see point 3.) lies in the type of molecule used for downregulating the activity of lysyl oxidase in the treatment of fibrosis.

11. In the board's judgement, no technical effect of this difference is derivable from the application as filed.

While anti-LOR-1 polyclonal sera were generated in the application (see page 48, lines 17 to 21), they have not been tested in any fibrosis model or compared to any of the lysyl oxidase inhibitors known from document D3.

12. Therefore the board considers that the technical problem to be solved by the claimed subject-matter can be formulated as the provision of an alternative lysyl oxidase inhibitor for use in treating fibrosis.

Obviousness of the claimed solution

13. The question to be answered in assessing obviousness is whether the skilled person, seeking to solve the technical problem formulated above and starting from the disclosure in document D3, would have modified the teaching in the closest prior art document in the light of other teachings in the prior art so as to arrive at the claimed solution without inventive effort.

14. In the board's view, the skilled person, faced with the problem of providing an alternative lysyl oxidase inhibitor for use in treating fibrosis, would have considered all known lysyl oxidase inhibitors.

15. Document D12 discloses such an inhibitor. Document D12 concerns a protein termed LOR-1 (see page 3, lines 7 to 12; page 8, lines 7 to 14; SEQ ID NO: 2) which belongs to the lysyl oxidase family of enzymes and catalyses the formation of covalent crosslinks between lysine residues on adjacent collagen or elastin fibrils (see page 8, lines 7 to 10). D12 also discloses the generation of anti-LOR-1 polyclonal antisera (see page 24, lines 17 to 21). It furthermore discloses that fibrotic liver tissues such as those observed in

Wilson's disease exhibit a strong increase in hepatocyte expression of LOR-1 (see page 27, lines 4 to 9; Figure 6d), that of four lysyl oxidase family members examined LOR-1 was the only one expressed in endothelial cells of blood vessels (see page 25, lines 25 to 30), and that antibodies directed at lysyl oxidase can be used to specifically inhibit lysyl oxidase activity when introduced into mammalian tissue (see page 9, lines 19 to 22). The LOR-1 protein of document D12 is identical to the LOR-1 protein of the present application (compare amino-acid sequence given in SEQ ID NO: 2 of document D12 and in SEQ ID NO: 2 of the present application).

16. In the board's judgement, document D12, in disclosing that LOR-1 is a lysyl oxidase which is expressed in fibrotic tissue and that an antibody that inhibits LOR-1 can be used to specifically inhibit lysyl oxidase activity when introduced into mammalian tissue, would have prompted the skilled person, when faced with the problem formulated above, to use such an anti-LOR-1 antibody for treating fibrosis.

17. An embodiment falling within the scope of claim 1 is thus obvious and the subject-matter of claim 1 therefore fails to meet the requirements of Article 56 EPC.

Concluding remarks

18. The sole claim request forming part of the appeal proceedings does not meet the requirements of Article 56 EPC. Accordingly, a patent cannot be granted on the basis of this request, and in the absence of another, allowable, claim request the appeal must be dismissed.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

I. Aperribay P. de Heij

Decision electronically authenticated