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Datasheet for the decision of 13 December 2011

Case Number: T 0583/09 - 3.3.08

Application Number: 00941494.7

Publication Number: 1194534

IPC: C12N 15/00, C07K 14/47, C12Q 1/68, G01N 33/50

Language of the proceedings: EN

Title of invention:
Novel genes encoding proteins having diagnostic, preventive, therapeutic, and other uses

Applicant:
MILLENNIUM PHARMACEUTICALS, INC.

Headword:
Novel genes/MILLENNIUM

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
"Added matter: all requests (yes)"

Decisions cited:
G 0010/93, T 0823/96, T 0727/00

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0583/09 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 13 December 2011

Appellant: (Applicant)
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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 22 October 2008 refusing European patent application No. 00941494.7 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman: M. Wieser
Members: B. Stolz
J. Geschwind

Summary of Facts and Submissions

I. The applicant (appellant) filed an appeal against the decision of the examining division to refuse European patent application No. EP00941494.7 pursuant to Article 97(2) EPC.

II. The examining division decided that neither the main request nor the auxiliary request before it met the requirements of Article 56 EPC.

III. The appellant requested that the decision under appeal be set aside, and a patent be granted on the basis of the main request or in the alternative on the basis of auxiliary requests 1 to 4, all newly filed with the grounds of appeal. It furthermore requested oral proceedings should the board be minded to refuse its main request.

IV. The board summoned the appellant to oral proceedings. A communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) dated 3 August 2011, annexed to the summons, informed the parties of the preliminary non-binding opinion of the board on some of the issues of the appeal proceedings. A substantial part of this communication (points 7 to 14, and 19) concerned issues under Article 123(2) EPC.

V. With letter dated 11 November 2011, the appellant informed the board that it would not attend oral proceedings.

VI. Oral proceedings were held on 13 December 2011, in the absence of the appellant.

VII. The claims of the main request relevant for this decision read:

"1.An isolated nucleic acid molecule selected from the group consisting of:
a) a nucleic acid molecule comprising a nucleotide sequence which is at least 80% identical to the nucleotide sequence as shown in SEQ ID NO: 59 or 60, or a complement thereof; and
b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 61 or 63, or a complement thereof.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:
a) a nucleic acid molecule comprising a nucleotide sequence which is at least 90% identical to the nucleotide sequence as shown in SEQ ID NO: 59 or 60, or a complement thereof;
b) a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence as shown in SEQ ID NO: 59 or 60, or a complement thereof; and
c) a nucleic acid molecule comprising a nucleotide sequence which is at least 98% identical to the nucleotide sequence as shown in SEQ ID NO: 59 or 60, or a complement thereof.

9. An isolated polypeptide selected from the group consisting of:
a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO: 61 or 63, wherein the fragment comprises at least 200 contiguous amino acids

of SEQ ID NO: 61 or 63, wherein the fragment has the ability to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix;

b) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 80% identical to a nucleic acid consisting of the nucleotide sequence as shown in SEQ ID NO: 59 or 60, or a complement thereof; and

c) a polypeptide comprising an amino acid sequence which is at least 80% identical to the amino acid sequence of SEQ ID NO: 61 or 63.

10. The isolated polypeptide of claim 9, selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence as shown in SEQ ID NO: 61 or 63;

b) a polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence as shown in SEQ ID NO: 61 or 63; and

c) a polypeptide comprising an amino acid sequence which is at least 98% identical to the amino acid sequence as shown in SEQ ID NO: 61 or 63.

13. An antibody or immunologically active portion thereof which specifically binds to a polypeptide selected from the group consisting of:

(a) the polypeptide of claim 9;

(b) the polypeptide of claim 10;

(c) the polypeptide of claim 11; and

(d) the polypeptide of claim 12

wherein the antibody is conjugated to a therapeutic substance, provided that the antibody is not an

antibody which specifically binds to the polypeptide of SEQ ID NO:8 of W000/753 17.

16. The antibody or immunologically active portion thereof of any one of claim 13 to 15, wherein the therapeutic substance is a cytotoxic agent.

17. The antibody or immunologically active portion thereof of claim 16, wherein the cytotoxic agent is an antimitotic agent.

19. A method for producing a polypeptide selected from the group consisting of:
a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 61 or 63;
b) a polypeptide comprising a fragment of the amino acid sequence of SEQ ID NO: 61 or 63, wherein the fragment comprises at least 200 contiguous amino acids of SEQ ID NO: 61 or 63, wherein the fragment has the ability to:
i) bind to hyaluronic acid; or
ii) bind to extracellular matrix; and
c) a polypeptide comprising an amino acid sequence which is at least 80% identical to the amino acid sequence as shown in SEQ ID NO: 61 or 63, the method comprising culturing the host cell of claim 6, 7 or 8 under conditions in which the polypeptide is expressed.

25. A method for modulating the ability of a polypeptide of any of claims 9 to 12 to:
i) bind to hyaluronic acid; or
ii) bind to extracellular matrix;

comprising contacting a polypeptide or a cell expressing a polypeptide of any of claims 9 to 12, with an antibody which specifically binds to the polypeptide in a sufficient concentration to modulate the ability of the polypeptide to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix.

26. An in vitro method for identifying a compound which modulates the ability of a polypeptide of any of claims 9 to 12 to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix;

comprising:

a) contacting a polypeptide of any of claims 9 to 12, with a test compound; and

b) determining the effect of the test compound on the ability of the polypeptide to

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix;

thereby identifying a compound which modulates the ability of the polypeptide to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix."

VIII. The claims of auxiliary request I differ from those of the main request by the fact that the claimed nucleic acid and polypeptide sequences are defined as consisting of, instead of comprising, the recited sequences. Thus, e.g. claim 1 reads:

"1.An isolated nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule consisting of a nucleotide sequence which is at least 80% identical to the nucleotide sequence as shown in SEQ ID NO: 59 or 60, or a complement thereof; and
b) a nucleic acid molecule which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 61 or 63, or a complement thereof." (emphasis added)

IX. The identical claims of auxiliary requests II and III relevant for this decision read:

"7. An isolated polypeptide consisting of the amino acid sequence of SEQ ID NO: 61 or 63, or a complement thereof.

8. An antibody or immunologically active portion thereof which specifically binds to a polypeptide of claim 7; wherein the antibody is conjugated to a therapeutic substance, provided that the antibody is not an antibody which specifically binds to the polypeptide of SEQ ID NO:8 of WO00/75317.

11. The antibody or immunologically active portion thereof of any one of claim 8 to 10, wherein the therapeutic substance is a cytotoxic agent.

12. The antibody or immunologically active portion thereof of claim 11, wherein the cytotoxic agent is an antimitotic agent.

13. An antibody or immunologically active portion thereof which specifically binds to a polypeptide consisting of an amino acid sequence of SEQ ID NO: 61 or 63, which is conjugated to a cytotoxic agent,

provided that the antibody is not an antibody which specifically binds to the polypeptide of SEQ ID NO:8 of WO00/75317.

20. A method for modulating the ability of a polypeptide of claim 7 to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix;

comprising contacting a polypeptide or a cell expressing a polypeptide of claim 7, with an antibody which specifically binds to the polypeptide in a sufficient concentration to modulate the ability of the polypeptide to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix.

21. An in vitro method for identifying a compound which modulates the ability of a polypeptide of claim 7 to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix;

comprising:

a) contacting a polypeptide of claim 7, with a test compound; and

b) determining the effect of the test compound on the ability of the polypeptide to

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix;

thereby identifying a compound which modulates the ability of the polypeptide to:

i) bind to hyaluronic acid; or

ii) bind to extracellular matrix."

X. Claims 11 to 13 of auxiliary request IV are identical with claims 11 to 13 of auxiliary requests II and III.

XI. Appellant's arguments, as far as they are relevant to the present decision, may be summarized as follows:

Basis for the amended claims could be found in the patent application as originally filed, mainly in the claims and on pages 2 to 4, 10, 14, 90 to 99, and 122 to 124.

Reasons for the decision

1. According to the Order of the decision G 10/93 of the Enlarged Board of Appeal (OJ EPO, 1995, page 172) "in an appeal from a decision of an examining division in which a European patent application was refused, the board of appeal has the power to examine whether the application or the invention to which it relates meets the requirements of the EPC. The same is true for requirements which the examining division did not take into consideration in the examination proceedings or which it regarded as having been met. If there is reason to believe that such requirement has not been met, the board shall include this ground in the proceedings". Thus, the board is not limited to the examination of the objections raised in the decision under appeal but has to examine whether the appellant's requests fulfil all the requirements of the EPC.

In a first step, the board is therefore examining whether the requests before it meet the requirements of Article 123(2) EPC.

Article 123(2) EPC

2. In order to determine whether or not the subject-matter of an amended claim extends beyond the content of the application as filed, it has to be examined whether that claim comprises technical information which a skilled person would not have clearly and unambiguously derived from the original application. The disclosure of such technical information can be explicit or implicit. The term "implicit disclosure" should not be construed to mean matter that does not belong to the content of the technical information provided by a document but may be rendered obvious on the basis of that content. The term "implicit disclosure" relates solely to matter which is not explicitly mentioned, but is a clear and unambiguous consequence of what is explicitly mentioned (decision T 823/96 of 28 January 1997; point 4.5).

Main request

3. The subject matter defined by SEQ ID NOs 59 to 61, and 63 is labelled "Tango 332" and discussed briefly in a paragraph bridging pages 9 and 10, and in more detail on pages 90 to 99 of the published international patent application.

The present application discloses not only Tango 332 but also several other unrelated molecules. Pertinent sections of the application relating to additional features of "Tango 332" and these other molecules can be found on pages 11 to 14, and 100 to 127.

4. Claims 1(a) and 2(a), (b), and (c), respectively, refer to nucleic acid molecules comprising nucleotide sequences with respectively 80, 90, 95, and 98% of identity with SEQ ID NOs 59 or 60.

A paragraph of the description discussing related sequences can be found on page 2, lines 24 to 30, where the following is explicitly stated: "The invention also features nucleic acid molecules which are at least 40%(or, 50%, 60%, 70%, 80%, 90%, 95%, or 98%) identical to the nucleotide sequence of any of SEQ ID NOs: 1, 2, 9, 10, 33, 34, 38, 39, 46, 47, 54, 55, 59, 60, 81, 82, and 92". In the board's view, this paragraph presents two lists of properties or features of the claimed subject matter, a first list of sequence identities and a second list of sequence numbers.

According to decision T 727/00 of 22 June 2001 (reasons, pt 1.1.4), the specific combination of one item from each of two lists of features results in subject matter which, although conceptually comprised in the application as filed, is not disclosed in the particular individual form. This decision is in line with established case law, and the board is convinced that this rationale equally applies to the case at issue.

Conceptually, any of the degrees of identity of the first list can be combined with any of the sequences of the second list. The board does however not regard this as a direct and unambiguous disclosure of the nucleic acid molecules of claim 1(a), i.e. of those molecules comprising a nucleotide sequence which is "at least 80% identical to the nucleotide sequence as shown in SEQ ID

IN: 59 or 60". The same applies to the specific combinations of features of claims 2(a), (b), and (c).

5. Similarly, the board cannot find basis for claims 9(a) and 19(b). The paragraphs of the description relating to polypeptide fragments (e.g. page 3, lines 20 to 24) present a first list of possible fragment lengths ("at least 8(10, 15, 20, 25, 30, 40, 50, 75, 100, 125, 150, or 200)") and a second list of polypeptides defined by SEQ ID numbers ("SEQ ID NOs: 3-8, 11-32, 35-37, 40-45, 48-53, 56-58, 61-63, 83-88, and 93-98"). This can however not be regarded as a direct and unambiguous disclosure of polypeptide fragments of SEQ ID NOs 61 or 63 of at least 200 amino acids in length.

Moreover, there is no disclosure of fragments of SEQ ID NOs 61 or 63 of at least 200 amino acids binding to hyaluronic acid or extracellular matrix. The sections of the description relating specifically to Tango 332 describe the presence of a domain binding to hyaluronan (p. 94, lines 8-9). There is however no mention of fragments of Tango 332 specifically binding to hyaluronan, let alone of fragments comprising at least 200 contiguous amino acids.

6. Regarding claims 9(c), 10(a), (b), and (c), and 19(c), respectively, directed to isolated polypeptides and a method for producing such, the board cannot find direct and unambiguous disclosure of polypeptides which are respectively and specifically at least 80% or 90% or 95% or 98% identical with SEQ ID NOs 61 or 63. The respective paragraph on page 4 (lines 3 to 6), and the last paragraph on page 111 each present a first list of

sequence identities and a second list of sequence numbers.

7. As a consequence of the lack of a proper basis for the polypeptides of claims 9 and 10, there is also no proper basis for claims 13, 16, and 17 directed to antibodies specifically binding to the polypeptides of these claims.

Moreover, there is no basis for claims 16 and 17, directed to such antibodies conjugated to a cytotoxic agent and an antimitotic agent, respectively (claims 16 and 17). Paragraphs of the description relating to antibodies conjugated to therapeutic substances contain lists of several therapeutic substances (cf. page 122, lines 17-18, "an antibody substance can be conjugated with a therapeutic moiety such as a cytotoxin, a therapeutic agent, or a radioactive metal ion"; cf. also page 122, line 25 to page 26, line 2, "Therapeutic agents include, antimetabolites (e.g. ...), alkylating agents (e.g. ...), anthracyclines (e.g. ...), antibiotics (e.g. ...), and anti-mitotic agents (e.g. ...).")(emphasis added). There is however no direct and unambiguous disclosure of the conjugation of specific antibodies selected from the many lists of antibodies (cf. pages 123 to 125) to specifically a cytotoxin or an antimitotic agent, both selected from lists of possible therapeutic substances.

8. Basis for claims 25 and 26, directed to methods for modulating the ability of any of the polypeptides with the features of claims 9 to 12 to bind to hyaluronic acid or extracellular matrix, is also not apparent from the application as filed. Original claims 21 and 22

provide basis for methods for identifying a compound which modulates the activity of a claimed polypeptide. The part of the description relating to Tango 332 provides numerous activities such as "establishment and maintenance of neural connections, cell-to-cell adhesion, tissue and extracellular matrix invasivity, and the like" (page 9, line 32 to page 10, line 1), cartilage organization, extracellular matrix organization, neural growth and branching, cell-to-cell and cell-to-matrix interactions (page 94, lines 13 to 16). It is also mentioned that the protein contains a pair of extracellular link domains indicating that this protein is also involved in HA binding. But there is no direct and unambiguous disclosure of methods in which modulation of the binding of any of the proteins of claims 9 to 12 to hyaluronic acid or extracellular matrix is assayed.

9. In view of the above mentioned deficiencies, the main request does not meet the requirements of Article 123(2) EPC.

Auxiliary request I

10. The claims of auxiliary request I differ from those of the main request by the fact that the claimed nucleic acid and polypeptide sequences are defined as consisting of, instead of comprising, the recited sequences (cf. section VIII). This has however no influence on the conclusions drawn by the board in relation to the objections under Article 123(2) EPC (cf. points 4 to 9 above). The objections raised in the preceding paragraphs against the claims of the main

request equally apply to the corresponding claims of auxiliary request I.

Auxiliary requests II and III.

11. Claims 11 to 13 of auxiliary requests II and III (cf. section IX above), refer to antibodies according to preceding claim 8, which are conjugated to a therapeutic substance and specifically bind to the polypeptides of claim 7, i.e. to the polypeptides consisting of the amino acid sequences of SEQ ID NO: 61 and 63. Basis for the antibodies of claim 8 can be derived from the paragraph beginning at page 123, line 28 and ending at page 124, line 2, in combination with paragraph 2 on page 126 stating that any of the antibody substances of the invention can be combined with a therapeutic moiety.

For the reasons already given in point 7, 2nd paragraph, above, there is no direct and unambiguous disclosure of antibodies binding to the polypeptides consisting of SEQ ID NOs 61 and 63, which are conjugated to a cytotoxic agent (claims 11 and 13) or an antimitotic agent (claim 12). The paragraph bridging pages 123 and 124 provides a first list of antibodies specifically binding to many different peptides and the second paragraph on page 122 provides a second list of possible therapeutic substances.

12. Regarding claims 20 and 21 (cf. section 9 above), the reasoning given under point 8 for claims 25 and 26 of the main request equally applies.

13. In view of these deficiencies, auxiliary requests II and III do not meet the requirements of Article 123(2) EPC.

Auxiliary request IV

14. Since claims 11 to 13 of auxiliary request IV are identical with claims 11 to 13 of auxiliary requests II and III, the above said (cf. point 11) equally applies, and auxiliary request IV does not meet the requirements of Article 123(2) EPC.

15. In conclusion, none of the requests on file complies with the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

V. Commare M. Wieser