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Datasheet for the decision of 24 February 2017

Case Number: T 1944/13 - 3.3.04

Application Number: 10185182.2

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Language of the proceedings: EN

Title of invention:
Antibodies that immunospecifically bind to BLyS

Applicant:
Human Genome Sciences, Inc.

Headword:
Anti-BLyS antibodies/HUMAN GENOME SCIENCES

Relevant legal provisions:
EPC Art. 76(1)

Keyword:
Divisional application - subject-matter extends beyond content of earlier application (yes)

Decisions cited:
T 0012/81, T 0783/09

Catchword:

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Case Number: T 1944/13 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 24 February 2017

Appellant: (Applicant)	Human Genome Sciences, Inc. 14200 Shady Grove Road Rockville, MD 20850 (US)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstrasse 3 81675 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 27 March 2013 refusing European patent application No. 10185182.2 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	A. Chakravarty
	P. de Heij

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. 10 185 182.2, entitled "*Antibodies that immunospecifically bind to BLyS*". The application is a divisional application of earlier application No. 01 946 365.2, published as WO 02/02641.

II. In the decision under appeal, the examining division held that claims 1 to 4 of the sole claim request did not meet the requirements of Article 76(1) EPC because their subject-matter was not directly and unambiguously derivable from the parent application as filed.

III. With the statement of grounds of appeal the appellant requested as a main request that the decision under appeal be set aside and that a patent be granted on the basis of the claim set filed on 3 February 2012 or, as an auxiliary request, on the basis of the claim set filed with the statement of grounds of appeal.

IV. Claim 1 of the main request reads:

"1. An antibody that neutralizes B Lymphocyte Stimulator Protein or a functional fragment thereof, wherein the antibody is

(i) a human antibody that binds B Lymphocyte Stimulator Protein, wherein the antibody comprises:

(a) an amino acid sequence that is at least 85% identical to residues 1-126 of SEQ ID NO: 1321; and

(b) an amino acid sequence that is at least 85% identical to residues 143-251 of SEQ ID NO: 1049;

(ii) a monoclonal antibody that competitively inhibits binding of the antibody of (i) to B Lymphocyte Stimulator Protein; or

(iii) a monoclonal antibody that reduces binding of the antibody of (i) to B Lymphocyte Stimulator Protein by an increment within a percentage range selected from the group consisting of:

(a) from 50% up to 60%;
(b) from 60% up to 70%;
(c) from 70% up to 80%;
(d) from 80% up to 90%; and
(e) from 90% up to 100%".

Claim 1 of the auxiliary request read:

"1. An antibody that immunospecifically binds to B Lymphocyte Stimulator Protein or a functional fragment thereof, wherein the antibody is

(i) a human antibody that binds B Lymphocyte Stimulator Protein, wherein the antibody comprises:

(a) an amino acid sequence that is at least 85% identical to residues 1-126 of SEQ ID NO: 1321; and
(b) an amino acid sequence that is at least 85% identical to residues 143-251 of SEQ ID NO: 1049;

(ii) a monoclonal antibody that competitively inhibits binding of the antibody of (i) to B Lymphocyte Stimulator Protein; or

(iii) a monoclonal antibody that reduces binding of the antibody of (i) to B Lymphocyte Stimulator Protein by

an increment within a percentage range selected from the group consisting of:

(a) from 50% up to 60%;
(b) from 60% up to 70%;
(c) from 70% up to 80%;
(d) from 80% up to 90%; and
(e) from 90% up to 100%".

V. The board issued a communication pursuant to Article 15(1) RPBA, setting out its preliminary appreciation of substantive and legal matters concerning the appeal.

VI. The appellant responded to the board's communication with a letter in which the request for oral proceedings was withdrawn and which also informed the board that they would not attend the scheduled oral proceedings.

VII. Oral proceedings before the board were held in the absence of the appellant in accordance with Article 116(1) EPC, first half sentence and Rule 115(2) EPC on 24 February 2017. At the end of the proceedings the Chairman announced the decision of the board.

VIII. The appellant's arguments relevant to the decision can be summarised as follows.

The parent application as filed, expressly disclosed each and every antibody that resulted from the free combination of the V_H domains disclosed in Table 1 with the V_L domains disclosed in Table 1. The parent application, for instance in paragraphs [009] and [0212], in fact contained the instruction to combine any of the V_H domains of Table 1 with any of the V_L domains of Table 1 into one antibody. There was ample

additional disclosure supporting this, for example, in connection with antibodies of the invention, it was disclosed that "*a VH domain of an amino acid sequence disclosed herein may be combined with a VL domain of an amino acid sequence disclosed herein, or other VL domains, to provide a VH/VL pairing representing an antigen-binding site of an antibody. Similarly, a VL domain of an amino acid sequence disclosed herein may be combined with a VH domain of an amino acid sequence disclosed herein, or other VH domains*" (see parent application, page 8, paragraphs [013] and [014]).

This was supported by the disclosure of the subsequent paragraph and made it clear that it was totally open with regard to which V_H domains and V_L domains could be combined in an antibody.

Claim 1 of the main request was also supported by paragraph [0225] of the parent application which disclosed antibodies that comprised or consisted of a V_L domain of one of the scFvs referred to in Table 1 combined with a V_H domain of one of the scFvs referred to in Table 1 or other V_H domain.

In summary, paragraphs [0013]/[0014] and [0225] as well as original claim 31 of the parent application contained explicit support for antibodies resulting from each and every combination of any V_H domain referred to in Table 1 with any V_L domain referred to in Table 1.

The examining division was wrong to hold that the claimed subject-matter was a combination that could only be arrived at by selecting from two lists (point 16 of the decision) because, as set out above, the

parent application explicitly disclosed the claimed subject-matter.

The examining division should have applied the law as explained in decision T 783/09 in which the board held that case-by-case determination was needed to assess under what circumstances the combination from two lists was actually disclosed. It was not mandatory that such a combination was always not disclosed. The present case differed from the "*two-list*" theory established by decision T 12/81 because it was accompanied by the specific instruction to the skilled reader that each and every combination was meant to be disclosed.

Reasons for the Decision

1. In view their absence at the oral proceedings, the appellant is treated as relying on the written case (Article 15(3) RPBA).

Main and auxiliary request

Articles 100(c) and 76(1) EPC: claim 1

2. Article 76(1) EPC provides that a European divisional application "*may be filed only in respect of subject-matter which does not extend beyond the content of the earlier application as filed*".

3. According to established case law of the boards of appeal, it is a requirement that the subject-matter of a divisional application is directly and unambiguously derivable from the earlier application as filed, taken as a whole and using common general knowledge at the

date of filing of the earlier application (see Case Law of the Boards of Appeal of the EPO, 8th edition, sections II.F.2.1, II.F.2.1.1 and II.E.1).

4. Claim 1 of both requests relates, in one aspect, to a human antibody that binds B Lymphocyte Stimulator Protein (BLyS), wherein the antibody comprises (a) an amino acid sequence identical to residues 1-126 of SEQ ID NO: 1321 and (b) an amino acid sequence that is identical to residues 143-251 of SEQ ID NO: 1049.

5. SEQ ID NO: 1321 is the amino acid sequence of an scFv (single-chain variable fragment) having clone ID I042A10 and residues 1-126 represent the V_H domain of this molecule (see application, Table 1, page 165). SEQ ID NO: 1049 is the amino acid sequence of an scFv having clone ID I014F02. Residues 143-251 represent the V_L domain of this molecule (see application, Table 1, page 158).

6. The issue to be decided in the present case is whether or not the above mentioned human antibody is disclosed in the earlier, parent, application as filed.

7. There is no direct individualised disclosure in the parent application as filed, of the antibody defined in point 4. above. A number of passages disclose antibodies containing combinations of V_H and V_L domains as a general concept. Paragraph [009] reads "*antibodies [...] that immunospecifically bind to a polypeptide or a polypeptide fragment of BLyS, said antibodies comprising, [...] a polypeptide having the amino acid sequence of any one of the V_H domains referred to in Table 1, below, and any one of the V_L domains referred to in Table 1*". This disclosure is echoed in paragraphs [013] to [015], [0212] and [0225], cited by the

appellant in the statement of grounds of appeal. For instance, paragraph [0225] reads "*The present invention also provides antibodies [...] that immunospecifically bind to a polypeptide or a polypeptide fragment of BLyS, wherein said antibodies comprise [...] a VH domain of one of the scFvs referred to in Table 1 combined with a VL domain of one of the scFvs referred to in Table 1, or other VL domain. [...]In a preferred embodiment, antibodies that immunospecifically bind to a polypeptide or a polypeptide fragment of BLyS, comprise, or alternatively consist of, a polypeptide having the amino acid sequence of a VH domain contained SEQ ID NOS: 1-46, 321-329, 834-872, 1563-1595, or 1881-1908 as disclosed in Table 1 and a VL domain contained in contained SEQ ID NOS: 1-46, 321-329, 834-872, 1563-1595, or 1881-1908 as disclosed in Table 1*".

8. Table 1, referred to in these passages, begins on page 290 and ends on page 349 of the parent application. It is entitled "*scFvs that Immunospecifically Bind to BLyS*" and contains a listing of 2128 scFVs according to their "*clone ID*" and provides the SEQ ID NO of the corresponding entry in the sequence listing and, *inter alia*, the amino acid positions of the V_H and V_L domains within each sequence.

9. The board is of the view that the skilled person reading the parent application, and in particular those passages mentioned above that relate to antibodies comprising combinations of V_H and V_L domains of various scFVs of Table 1, would conclude that the parent application disclosed BLyS-binding antibodies containing combinations of V_H and V_L domains selected from the separate scFVs listed in Table 1, as a general

concept. However, in the absence of a disclosure, pointer or preference in the parent application, the board considers that the skilled reader would not consider an antibody comprising the single, specific combination of the particular V_H and V_L domains claimed (see point 4., above) to be directly and unambiguously disclosed (cf. Case Law of the Boards of Appeal of the European Patent Office, 8th edition, II.E. 1.4.1 and 1.4.2).

10. The appellant argued that the case law relating to the "*two lists*" principle, established by decision T 12/81, did not apply to the present case, because the parent application contained an explicit disclosure for the combinations of any V_H domain of Table 1 with any V_L domain of Table 1.

10.1 As discussed above, the disclosure that such domains from different scFVs that bind BLyS can be combined in a different antibody having also having BLyS specificity is found in the various passages in the description of the parent application cited above, i.e. paragraphs [009], [013] to [015], [0212] and [0225]. These paragraphs disclose that antibodies that immunospecifically bind to BLyS can be constructed by combining any V_H chosen from Table 1 with any V_L chosen from the same Table.

10.2 The board holds that this disclosure amounts to no more than a teaching that the V_H and V_L domains of each scFV may be regarded as lists from which a selection is to be made in order to obtain a BLyS-binding antibody. However, it does not amount to a disclosure of individual antibodies comprising each and every possible combination and in particular, not of an antibody comprising an amino acid identical to residues

1-126 of SEQ ID NO: 1321 and an amino acid sequence identical to residues 143-251 of SEQ ID NO: 1049.

11. The appellant further considered the finding of this board, in a different composition, in decision T 783/09 as applicable to the case at hand. In that case, the board advocated a case-by-case determination of whether any particular combination of items disclosed in two lists, was also disclosed individually.

11.1 The present board agrees with the finding in decision T 783/09 that the disclosure of "*subject-matter individualised from lists has to be determined according to the circumstances of each specific case by ultimately answering the question whether or not the skilled person would clearly and unambiguously derive the subject-matter at issue from the document as a whole*" (see point 5.6 of the reasons). In decision T 783/09, the board identified a direct and unambiguous disclosure of certain "*very preferred*" combinations (see 5.4 of the reasons) and concluded that the skilled person would directly and unambiguously recognise forty-four individual combinations. However, in the case at hand, the board has been unable to identify any disclosure or pointer in the parent application that would lead the skilled person to directly and unambiguously recognise an antibody comprising amino acids 1-126 of SEQ ID NO: 1321 and amino acid 143-251 of SEQ ID NO: 1049 as claimed. Indeed, an antibody having this combination does not even fall within those as disclosed as more preferred in paragraph [0249] of the parent application.

12. In view of the above, the board concludes that the subject-matter of claim 1 of the main and auxiliary request is not directly and unambiguously derivable

from the parent application as a whole, taking into account common general knowledge in the art, and does not meet the requirements of Article 76(1) EPC. Hence no request is allowable.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated