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Datasheet for the decision of 19 June 2008

Case Number: T 0724/05 - 3.3.04

Application Number: 90917366.8

Publication Number: 0497904

IPC: A61K 39/395

Language of the proceedings: EN

Title of invention:
Methods and transgenic plants for the production of plant-produced gylcopolypeptide multimers

Patentee:
THE SCRIPPS RESEARCH INSTITUTE

Opponents:
01: MPB Cologne GmbH Molecular Plant & Protein Biotechnology
02: MERISTEM THERAPEUTICS

Headword:
Glycopolypeptide multimers/SCRIPPS

Relevant legal provisions:
EPC Art. 54(1)-(3), 56, 83, 88, 89, 123(2)(3)

Relevant legal provisions (EPC 1973):
EPC Art. 87

Keyword:
"Representation of Respondent I (no)"
"Added subject-matter (no)"
"Priority right, novelty, inventive step, sufficiency of disclosure (yes)"

Decisions cited:
G 0004/88, G 0002/04, T 0019/90, T 0659/92, T 0792/00, T 0006/05, T 0677/05

Catchword:
see points 1 to 8 of the reasons

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0724/05 **-** 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 19 June 2008

Appellant: (Patent Proprietor)
THE SCRIPPS RESEARCH INSTITUTE
10550 North Torrey Pines Road
La Jolla
CA 92037 (US)

Representative:
Fisher, Adrian John
CARPMAELS & RANSFORD
43-45 Bloomsbury Square
London WC1A 2RA (GB)

Respondent I: (Opponent 01)
MPB Cologne GmbH Molecular Plant & Protein Biotechnology
Neurather Ring 1
D-51063 Köln (DE)

Respondent II: (Opponent 02)
MERISTEM THERAPEUTICS
8 rue des Frères Lumière
F-63100 Clermont-Ferrand (FR)

Representative:
Colombet, Alain André
Cabinet Lavoix
56 Avenue de Royat
B.P. 27
F-63401 Chamalieres Cedex (FR)

Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 23 February 2005 revoking European patent No. 0497904 pursuant to Article 102(1) EPC 1973.

Composition of the Board:

Chair: U. Kinkeldey
Members: M. Wieser
D. S. Rogers

Summary of Facts and Submissions

I. The appeal was lodged by the Patent Proprietor (Appellant) against the decision of the Opposition Division, whereby the European patent No. 0 497 904, published as WO 91/06 320, was revoked pursuant to Article 102(1) EPC 1973. The patent claims priority from two documents (US 427,765; 27 October 1989 and US 591,823; 2 October 1990).

II. The patent had been opposed by Opponent 01 (Respondent I) and Opponent 02 (Respondent II) under Article 100(a), 100(b) and 100(c) EPC 1973.

III. The Opposition Division decided that the subject-matter of claim 1 of each of the main request and of auxiliary request 2 before them lacked novelty (Article 54 EPC 1973). Moreover, they decided, that the subject-matter of claim 1 of each of auxiliary request 1 and 3 was not clear contrary to the requirements of Article 84 EPC 1973. Finally, they decided that the subject-matter of claim 1 of auxiliary request 4 violated Article 123(2) EPC 1973 and that the subject-matter of claim 1 of auxiliary request 5, which was found not to be entitled to the first of two claimed priority dates, lacked novelty (Article 54(3) EPC 1973).

IV. The Board expressed its preliminary opinion in a communication dated 9 November 2007.

Oral proceedings were held on 19 June 2008 in the absence of Respondent II, who had informed the Board that he would not attend.

V. The Appellant requested that the decision under appeal be set aside and the patent be maintained in amended form on the basis of claims 1 to 8 of the new main request submitted at the oral proceedings.

Respondents I and II requested in writing that the appeal be dismissed.

VI. Claims 1, 2, 3 and 8 of Appellant's new main request read as follows:

"1. A method of producing an immunologically active glycosylated immunoglobulin molecule free of sialic acid residues, comprising an oligosaccharide having a core portion and N-acetylglucosamine-containing outer branches, said method comprising:

(a) introducing into the genome of a first member of a plant species a first mammalian gene encoding an immunoglobulin heavy chain including its leader sequence forming a secretion signal, to produce a first transformant;

(b) introducing into the genome of a second member of said plant species a second mammalian gene encoding an immunoglobulin light chain including its leader sequence forming a secretion signal, to produce a second transformant;

(c) sexually crossing said first and second transformants to generate a progeny population;

(d) isolating from said progeny population a transgenic plant species producing a biologically active multimeric protein; and

(e) recovering from said transgenic plant species a composition comprising said biologically active multimeric protein and plant material.

2. A method of producing a biologically active heterodimeric antibody, comprising:

(a) introducing into the genome of a first member of a plant species a first mammalian gene encoding an immunoglobulin heavy chain including its leader sequence forming a secretion signal, to produce a first transformant;

(b) introducing into the genome of a second member of said plant species a second mammalian gene encoding an immunoglobulin light chain including its leader sequence forming a secretion signal, to produce a second transformant;

(c) sexually crossing said first and second transformants to generate a progeny population;

(d) isolating from said progeny population a transgenic plant species producing a heterodimeric antibody; and

(e) isolating said heterodimeric antibody from said transgenic plant species.

3. A transgenic plant comprising:

(a) plant cells containing a first mammalian gene encoding an immunoglobulin heavy chain including its leader sequence forming a secretion signal and a second mammalian gene encoding an immunoglobulin light chain including its leader sequence forming a secretion signal; and

(b) immunoglobulin molecules encoded by said genes, said immunoglobulin molecules comprising an oligosaccharide having a core portion and N-acetylglucosamine-containing outer branches, and being free of sialic acid residues.

8. A method for making a transgenic plant capable of producing a heterodimeric antibody, comprising:

(a) introducing into the genome of a first member of a plant species a first mammalian gene encoding an immunologically active immunoglobulin heavy chain including its leader sequence forming a secretion signal, to produce a first transformant;

(b) introducing into the genome of a second member of said plant species a second mammalian gene encoding an immunoglobulin light chain including its leader sequence forming a secretion signal, to produce a second transformant;

(c) generating from said first and second transformants a progeny population; and

(d) isolating from said progeny population a transgenic plant species producing an immunoglobulin molecule."

Dependent claims 4 to 7 referred to preferred embodiments of the transgenic plant according to claim 3.

VII. The present decision refers to the following documents:

(5) Inaugural-Dissertation, Klaus Düring, Köln 1988

(6) Nature, vol.342, 2 November 1989, pages 76 to 78

VIII. The relevant submissions made by the Appellant may be summarised as follows:

One day before the oral proceedings the Appellant had obtained a copy of a document dated 13 September 2002, entitled "Übertragungsvertrag", between Respondent I and Dr. Düring, (hereafter, "the Transfer Contract"). The Transfer Contract appeared to be a contract transferring all of Respondent I's intellectual property rights to Dr. Düring. This document indicated that Respondent I was insolvent as it was signed on behalf of Respondent I by a Mr. Jauch, who is described in the Transfer Contract as an "Insolvenzverwalter" (that is as an insolvency practitioner), and the first sentence of the preamble states "Über das Vermögen des Veräusserers ist das Insolvenzverfahren eröffnet" ("An insolvency procedure has been opened against the assets of the seller").It had therefore to be clarified if the representative present at the oral proceedings to represent Respondent I was indeed still representing Respondent I, and whether Respondent I still existed.

A copy of the Transfer Contract was handed over to the Board.

The Appellant argued that the Transfer Contract contained no explicit mention of a transfer of Respondent I's opponent status. In addition opponent status in proceedings before the EPO was not, in itself, an intellectual property right and so was not included under the term "Intellectual Property" referred to in point §1 of the Transfer Contract ("Vertragsgegenstand ist das gesamte geistige Eigentum (Intellectual Property) einschliesslich aller in Zusammenhang damit stehende Rechte und Schutzrechte des Veräußerers"). Thus there was no implicit reference to Respondent I's opponent status in the Transfer Contract. The Appellant also pointed out that the oral proceedings before the opposition division took place about 2 years after the signing of the Transfer Contract. At oral proceedings before the opposition division Dr. Düring was present as Respondent II's technical expert, not as a party in his own right.

The subject-matter of claims 1 to 8 of the new main request had a basis in the application as published (Article 123(2) EPC) and was entitled to claim priority from the first priority document (US 427,765; 27 October 1989).

The methods according to claims 1, 2 and 8 and the transgenic plant according to claim 3 were not disclosed in the prior art documents on file and were therefore novel. The closest state of the art was represented by document (5). Neither this document nor any other document on file contained any disclosure or

even suggestion that would have allowed a skilled person to arrive at the subject-matter of claims 1 to 8 in an obvious way. The patent, by way of detailed examples, disclosed the invention as required by Article 83 EPC.

IX. The relevant submissions made by the representative present at the oral proceedings to represent Respondent I, may be summarised as follows:

In a written submission dated on 18 April 2008, that purported to be filed on behalf of Respondent I, the representative argued that the claims of Appellant's request did not meet the requirements of Articles 54, 56 and 83 EPC. For the detailed facts and evidence the Board was referred to the notice of opposition. With regard to the issue of inventive step, he additionally referred to WO 87/00 865, a document cited in the International Search Report of the patent in suit.

At the oral proceedings before the Board on 19 June 2008, the representative stated that he had only become aware of the Transfer Contract the week before. He argued that the Transfer Contract transferred Respondent I's opponent status to Dr. Düring, in accordance with the requirements set out in the decision of the Enlarged Board of Appeal G 4/88 (OJ EPO 1989, 480), and that he was now representing Dr Düring. The representative present at the oral proceedings to represent Respondent I and Dr. Düring confirmed that, although the situation was unclear, the insolvency proceedings against Respondent I were still continuing and that Respondent I still existed.

The Transfer Contract transferred all of Respondent I's intellectual property rights to Dr. Düring. Although opponent status was not explicitly mentioned, the Transfer Contract also transferred Respondent I's opponent status in the present case to Dr. Düring, the opponent status being covered by the term "Intellectual Property" as used in the Transfer Contract. Accordingly, the representative authorized by Respondent I, was entitled to represent Dr. Düring before the Board of Appeal and that he was no longer representing Respondent I.

X. Respondent II, in his only submission in writing, dated 23 January 2006, argued that the subject-matter of the Appellant's then pending main request, which corresponded to the claims as granted, was not novel in the light of the disclosure in document (5). Moreover, he questioned whether the claims of this main request could validly claim priority from the first priority document (US 427,765; 27 October 1989). If this was not so, Appellant's own scientific publication, document (6), was considered to anticipate the claimed subject-matter. Finally, the patent did not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 83 EPC).

Respondent II did not file any submission dealing with the subject-matter of the claims of Appellant's actual main request, which, except for the numbering of the claims, was identical to auxiliary request 4, filed with the statement of the grounds for appeal dated 4 July 2005.

Reasons for the decision

Representation of Respondent I

1. The question has to be answered whether the Transfer Contract transfers Respondent I's opponent status to Dr. Düring.

2. Opponent status is not freely transferable (see decision of The Enlarged Board of Appeal G 2/04, OJ EPO 2005, 549; point I.(a) of the Order). However, a transfer of opponent status has been recognised by the Boards of Appeal in the following cases:

   (i) to heirs of an Opponent (implied from Rule 84(2)EPC, formerly Rule 60(2)EPC 1973);

   (ii) by analogy to heirs, to universal successors in law (see decision G 4/88, OJ EPO 1989, 480, point 4 and decision T 6/05, of 9 October 2007, point 1.6.3);

   (iii) if all of the assets of a business are transferred (see decision G 4/88 (supra), point 6 and decision T 659/92, OJ EPO 1995, 519, point 2);

   or

   (iv) as part of the opponent's business assets together with the assets in the interests of which the opposition was filed (see decision G 4/88 (supra), Order).

3. In the present case neither (i) nor (ii) above apply. From the terms of the Transfer Contract it is not evident that all of the assets of Respondent I were transferred to Dr Düring, thus (iii) above does not apply.

4. For the Board to make a finding that the opponent status of Respondent I was transferred to Dr. Düring the Board must therefore be satisfied that the facts of the present case fall under (iv) above.

As a preliminary point the Board needs to consider whether the assets transferred to Dr. Düring by the Transfer Contract are "assets in the interests of which the opposition was filed".

5. Paragraph 1 of the Transfer Contract reads:

"Vertragsgegenstand ist das gesamte geistige Eigentum (Intellectual Property) einschließlich aller in Zusammenhang damit stehende Rechte und Schutzrechte des Veräußerers."

Rights relating to "Intellectual property" are exclusionary rights over immaterial goods. The examples given in paragraph 1(a) to (f) of the Transfer Contract, namely inventions, patents, utility models, trade marks, copyright, technical and/or scientific trade secrets and rights to intellectual property of third persons (licences) are non-exhaustive examples of rights falling within this definition.

Opponent status, which is not an exclusionary right over immaterial goods, but rather a legal remedy, is not mentioned in paragraph 1(a) to (f).

6. At the oral proceedings Dr. Düring argued, that paragraph 1 of the Transfer Contract states that rights to "Intellectual Property" contain, but are not restricted to, the assets exemplified in points (a) to (f), and that it was his understanding of the Transfer contract that opponent status was included therein ("Hierunter fallen insbesondere, aber nicht ausschließlich ...").

In the light of the well established definition of rights to "Intellectual Property" and considering that the Transfer Contract itself explicitly lists various examples of intellectual property assets falling within this definition, the Board interprets the Transfer Contract as not covering opponent status, as this is neither explicitly listed, nor does it fall within said definition.

7. The Board is not in a position to determine whether any of the assts named in the Transfer Contract were "assets in the interests of which the opposition was filed" (cf decision T 677/05 of 26 June 2007; point 1).

Thus the Board is not prepared to conclude, in the absence of any information whatsoever on the substance of the rights transferred, that the term "Intellectual Property" referred to in the Transfer Contract inevitably includes those assets of Respondent I "... in the interests of which the opposition was filed".

8. Having reached this decision, the Board finds that the opponent status of Respondent I has not been transferred to Dr. Düring. Thus Dr. Düring may not participate in, nor be represented in this appeal with the status of a party in the sense of Article 107 EPC.

Amendments - Article 123(2) and (3) EPC

9. The subject-matter of claims 1, 2, 3, 7 and 8 is based on pages 84 to 93 and page 103, lines 29 to 34 of the application as published, where the construction of expression vectors containing heavy- and light-chain genes, the introduction of these vectors into tobacco plants, the production of a progeny expressing both, heavy- and light-chains and the isolation of biologically active antibodies from plants of this progeny population is described.

Claims 4 to 6 are based on claims 67 to 69 of the published application.

10. While claims 1 to 8 are not restricted to the production of (or to a transgenic plant comprising) a specific immunoglobulin, pages 69 onwards of the published application refer to experiments using genes coding for the heavy- and light-chain of a specific antibody derived from hybridoma cell line 6D4. However, it is evident that the teaching is not restricted to this specific embodiment. The specific nucleotide sequence of the genes used in the examples of the published application is neither a feature that is inextricably linked with further features of the disclosed method, nor is there any clearly recognisable

functional or structural relationship with said further features.

Thus in accordance with the established case law of the Boards of Appeal, amended claims 1, 2, 3, 7 and 8 are allowable under Article 123(2) EPC (see Case Law of the Boards of Appeal of the EPO, 5th Edition 2006, chapter III.A.1; page 240, last paragraph, English version).

11. By defining that the genes encoding the heavy- and light-chains include their own immunoglobulin leader sequences, the scope of protection of the claims has been reduced with regard to the claims as granted. Thus, the requirements of Article 123(3) EPC are met.

Novelty - Article 54(1) to (3) EPC

12. The relevant parts of the application as published, that have been identified in point (10) above to form the basis for the subject-matter of claims 1 to 8 (Article 123(2) EPC), are found verbatim in the first priority document (US 427,765; 27 October 1989)(see pages 52 to 61, page 71, line 32 to page 72, line 2 and claims 27 to 29). Claims 1 to 8 can therefore validly claim priority from US 427,765; 27 October 1989) (Articles 87 EPC 1973 and Articles 88 and 89 EPC).

Accordingly, document (6), published 2 November 1989, does not belong to the state of the art.

13. Respondent II's argument that the patent in suit cannot validly claim any priority date as it refers to two priority documents, one of which being a continuation-

in part of the other, has no basis in the EPC. Both priority dates lie within one year before the International filing date of the patent in suit. Therefore, the requirements of Article 87(1)EPC 1973 are fulfilled.

14. The subject-matter of claims 1 to 8 is not disclosed in document (5) or in any other prior art document on file (see "inventive step" below).

The requirements of Article 54(1) to (3) EPC are thus fulfilled.

Inventive step - Article 56 EPC

15. Document (5) represents the closest state of the art. This dissertation reports the expression of the anti-NP antibody B1-8 in ***Nicotiana tabacum***, using a dual cassette ***Agrobacterium*** expression vector. The heavy chain coding sequence and the light chain coding sequence were each fused to a sequence encoding the barley α-amylase secretion signal. Tobacco leaf disks were transformed with the vectors using conventional technology, and whole plants were subsequently regenerated. The detection of antigen-binding antibody by Western Blot of plant material purified by affinity chromatography is reported on pages 57 to 58 and 112 to 118).

16. The problem underlying the patent in suit is seen in the provision of an improved method for producing an immunologically active immunoglobulin in a plant and of a transgenic plant produced thereby. The method allows higher amounts of the desired product to be obtained.

17. The experimental part of the patent (starting on page 24) contains sufficient data and results to convince the Board that this problem has indeed been solved by the subject-matter of claims 1 to 8.

18. The method of claim 1 for producing an immunologically active glycosilated immunoglobulin molecule, the method of claim 2 for producing a biologically active heterodimeric antibody and the method of claim 8 for making a transgenic plant, are distinguished from the disclosure in document (5) by the following features:

The mammalian gene encoding an immunoglobulin heavy chain and the mammalian gene encoding an immunoglobulin light chain, each including its own immunoglobulin leader sequence, are introduced in different first and second members of a plant species. Said first and second transformants are sexually crossed to generate a progeny population and the desired molecule is isolated from said progeny.

19. The transgenic plant of claim 3 is distinguished from the plants obtained by the method disclosed in document (5) in so far as it contains a first mammalian gene encoding an immunoglobulin heavy chain and a second mammalian gene encoding an immunoglobulin light chain, each including its own immunoglobulin leader sequence.

20. Neither document (5) itself nor any of the other prior art documents on file contains any information that would prompt a skilled person to amend the teaching disclosed in the closest prior art document and to arrive at the subject-matter of claims 1 to 8 in an obvious way.

Accordingly the requirements of Article 56 EPC are met.

Sufficiency of disclosure - Article 83 EPC

21. When examining if the patent specification as a whole meets the requirements of Article 83 EPC, the Board must be satisfied firstly, that the patent specification places the skilled person in possession of at least one way of putting the claimed invention into practice, and secondly that the skilled person can put the invention into practice over the whole scope of the claim (decision T 792/00 of 2 July 2002; point 2).

22. In the light of the disclosure in the examples (starting on page 24 of the patent), the Board is satisfied that the patent specification places the skilled person in possession of at least one way of putting the claimed invention into practice.

23. As regards the question if the patent specification places a skilled person in a position to carry out the invention over the whole scope claimed, it has to be examined if the patent specification as a whole contains sufficient information to allow the skilled reader to obtain immunologically active immunoglobulins and transgenic plants different from the specific ones disclosed in the examples.

The Board is not aware of any evidence showing that this aim cannot be achieved when following the teaching of the patent specification.

A patent may only be objected to for lack of sufficient disclosure if there are serious doubts, substantiated

by verifiable facts. The mere fact that a claim is broad is not in itself a ground for considering the patent as not complying with the requirements of sufficient disclosure under Article 83 EPC (decision T 19/90, OJ EPO 1990, 476; point 3.3).

24. The Board considers that the patent discloses the invention in a manner sufficiently clear and complete for it to be carried by a person skilled in the art. The requirements of Article 83 EPC are met.

Order

For these reasons it is decided:

The case is remitted to the department of first instance with the order to maintain the patent in the following version:

Claims 1 to 8 of the main request, filed on 19 June 2008 during the oral proceedings;

Description, pages 1 to 44, filed on 19 June 2008 during the oral proceedings; and

Figures 1 to 10, filed on 19 June 2008 during the oral proceedings.

Registrar: Chair:

P. Cremona U. Kinkeldey