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**Datasheet for the decision
of 16 December 2009**

Case Number: T 0502/08 - 3.3.08

Application Number: 97914794.9

Publication Number: 0894143

IPC: C07K 14/20

Language of the proceedings: EN

Title of invention:

VMP-Like sequences of pathogenic borrelia

Patentee:

BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM

Opponent:

MIKROGEN molekularbiologische Entwicklungs-GmbH

Headword:

Borrelia/UNIVERSITY OF TEXAS

Relevant legal provisions:

EPC Art. 56

Relevant legal provisions (EPC 1973):

-

Keyword:

"Inventive step (yes)"

Decisions cited:

-

Catchword:

-



Case Number: T 0502/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 16 December 2009

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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
14 January 2008 concerning maintenance of
European patent No. 0894143 in amended form.

Composition of the Board:

Chairman: L. Galligani
Members: T. J. H. Mennessier
C. Heath

Summary of Facts and Submissions

- I. The opponent (appellant) lodged an appeal against the interlocutory decision of the opposition division dated 14 January 2008, whereby European patent No. 0 894 143, which had been granted on European application No. 97 914 794.9, published as the international application WO 97/31123, was maintained in an amended form on the basis of the auxiliary request (claims 1 to 44) filed at the oral proceedings of 19 November 2007. The auxiliary request corresponded exactly to claims 2 to 45 as granted with claim 1 as granted being replaced by dependent claim 44 as granted.

- II. The patent had been opposed on the grounds as set forth in Articles 100(a), (b) and (c) EPC that (i) the invention was neither new (Article 54 EPC) nor inventive (Article 56 EPC), (ii) the invention was not sufficiently disclosed (Article 83 EPC) and (iii) the patent contained subject-matter which extended beyond the content of the application as filed (Article 123(2) EPC).

- III. The statement of grounds of appeal was filed on 9 May 2008. The appellant argued that the auxiliary request accepted by the opposition division did not comply with the requirements of Articles 54, 56, 83, 84 and 123(2) EPC. A new document D13 (see Section X, *infra*), was relied upon in support of the objections of lack of novelty and inventive step.

- IV. The patent proprietor (respondent) replied with a letter sent on 9 October 2008. It was argued that the opponent's statement of grounds largely relied on late

filed facts and evidence. It was requested that the newly filed document not be introduced into the appeal proceedings.

- V. Together with a summons to oral proceedings, the board on 16 April 2009 issued a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) with an outline of the issues to be discussed at the upcoming oral proceedings.
- VI. In reply to that communication, both parties on 19 June 2009 filed additional submissions which were accompanied, as regards the respondent's submissions, by four auxiliary requests (1 to 4) and, as regards the appellant's submissions, by a new document.
- VII. Oral proceedings took place as scheduled on 21 July 2009. After a discussion on the main request, the latter was withdrawn and auxiliary request 1 filed on 19 June 2009 became the new main request (claims 1 to 42) with independent claim 2 reading as follows:
- "2. An isolated nucleic acid segment comprising
(a) the nucleic acid sequence of SEQ ID NO:1, or
(b) the complement of (a), or
(c) 20 contiguous bases of SEQ ID NO:1, capable of hybridizing to the complement of nucleic acid sequence of SEQ ID NO:1 under conditions of high stringencies,
or
(d) the complement of (c) capable of hybridizing to the nucleic acid sequence of SEQ ID NO:1 under conditions of high stringencies."

During the discussion of the main request, in particular the question of how to interpret claim 2(c) and (d), the issue of whether the interpretation advanced by the patentee could find support in the application as originally filed became relevant. The respondent requested that the case be referred back to the first instance for a discussion on this point, while the appellant preferred the issue to be discussed in these proceedings. After deliberation, the board decided to adjourn the oral proceedings to 16 December 2009. The respondent was requested to provide by 15 September 2009 in respect of Article 123(2) EPC statements in support of each and every claim of the main request while the appellant was requested to provide by the same date a detailed list of all objections against the claims of the main request.

VIII. As requested, both parties on 15 September 2009 filed additional submissions to which they replied reciprocally on 16 November 2009. The respondent's reply was accompanied by a new auxiliary request 1 (claims 1 to 42) with claim 2 reading:

"2. An isolated nucleic acid segment comprising
(a) the nucleic acid sequence of SEQ ID NO:1, or
(b) the complement of (a), or
(c) 20 contiguous bases of SEQ ID NO:1, **the nucleic acid segment being** capable of hybridizing to the complement of nucleic acid sequence of SEQ ID NO:1 under conditions of high stringencies, or
(d) the complement of (c) capable of hybridizing to the nucleic acid sequence of SEQ ID NO:1 under conditions of high stringencies." (emphasis added by the board)

IX. The second oral proceedings took place on 16 December 2009. Claim 2, items c) and d) of the main request then on file, was discussed in respect of compliance with Article 123(2) EPC. After deliberation, the board came to the conclusion that items c) and d) of claim 2 did not comply with Article 123(2) EPC. In view of the fact that auxiliary request 1 as filed by letter of 16 November 2009, and auxiliary request 2 and 3 of 19 June 2009 had the same problem, these requests were not further discussed, and the respondent filed a new auxiliary request 4 to replace auxiliary request 4 of 19 June 2009 and withdrew all the previous requests then on file, new auxiliary request 4 becoming its sole request. The appellant indicated that it had no objections under Articles 54, 83, 84 and 123 EPC to be made in respect of auxiliary request 4. As regards the compliance of the request with Article 56 EPC, the appellant only stated that it relied upon its written submissions while the respondent made no comments.

The sole request on file (auxiliary request 4) consisted of 17 claims, of which claims 1 and 2 read as follows:

"1. An isolated immunogenic polypeptide
(a) having at least 85% homology to the amino acid sequence of SEQ ID NO:2; and
(b) which specifically binds with antibodies raised against a polypeptide having the amino acid sequence of SEQ ID NO:2."

"2. An isolated nucleic acid segment comprising
(a) the nucleic acid sequence of SEQ ID NO:1, or
(b) the complement of (a)."

Claims 3 to 6 were dependent on claim 2 and directed to particular embodiments thereof. Claim 7 was directed to a method of using a DNA segment of any one of claims 2 to 6 to produce a polypeptide.

Claim 8 was directed to an isolated immunogenic polypeptide encoded by a nucleic acid according to any one of claims 2 to 6. Claim 9 was dependent on claim 8 and directed to a particular embodiment thereof.

Claim 10 was directed to a protein composition comprising the polypeptide of claim 8 or 9. Claim 11 was dependent on claim 10 and directed to a particular embodiment thereof. Claim 12 was directed to a composition of claim 10 or 11 for use in a method of generating an immune response.

Claim 13 was directed to a purified antibody that specifically binds to the polypeptide of claim 9. Claim 14 was dependent on claim 13 and directed to a particular embodiment thereof. Claim 15 was directed to an in vitro method of diagnosing Lyme disease comprising probing a sample from a subject for the presence of a nucleic acid segment of any one of claims 2 to 6, a polypeptide of claims 8 to 9, or an antibody that binds immunologically to a polypeptide of claim 9. Claim 16 was directed to an in vitro method of assaying for *Borrelia* infection comprising obtaining an antibody that binds immunologically to a polypeptide of claim 9 or a polypeptide that binds immunologically to such an antibody. Claim 17 was directed to an immunodetection kit comprising one or more polypeptides

of any one of claims 8 to 9 or an antibody that binds to a polypeptide of any one of claims 8 to 9.

X. The following documents are referred to in the present decision:

(D4c) Compilation of NCBI extracts with a comparison of sequence SEQ ID NO:2 with a variety of Vmp amino acid sequences of *Borrelia hermsii* (filed by the appellant-opponent with the notice of opposition)

(D6) Carol J. Carter et al., *Infection and Immunity*, Vol. 62, 1994, Pages 2792 to 2799

(D13) Blanca I. Restrepo and Alan G. Barbour, *Cell*, Vol. 78, 9 September 1994, Pages 867 to 876

XI. The submissions made by the appellant, insofar as they are relevant to the present decision, may be summarised as follows.

Compliance with Article 56 EPC

Document D13 represented the closest state of the art. It described the antigen diversity of *Borrelia hermsii* and showed that the *vmp*-gene thereof was located on linear plasmids of 28 to 32 kb.

In view of document D13, the technical problem could be seen as the identification of similar genes and of the correspondingly encoded proteins in other bacteria. Document D13 suggested that similar genes could be found in *Borrelia burgdorferi*. This was confirmed by document D6, which pointed to the similarities of the

surface proteins of *B. burgdorferi* with those of *B. hermsii*.

Thus, looking for corresponding plasmids, which contained sequences encoding Vmp-like proteins, was for the skilled person an easy matter. The sequencing of such proteins would have been routine at the relevant filing date. Given the breadth of the claims the respondent could not rely on a technical effect in respect of the whole scope of the claims.

- XII. The submissions made by the respondent, insofar as they are relevant to the present decision, may be summarised as follows:

Compliance with Article 56 EPC

Nowhere in document D13 taken as the closest state of the art was a pointer derivable therefrom to *Borrelia burgdorferi*, let alone to *vls* sequences, as provided by the present invention. The document did not suggest the existence of any related surface determinant beyond the *Borrelia hermsii* Vmp proteins, let alone to the existence of the recombination system of *B. burgdorferi*.

Document D6 stressed similarities between Vmp33 of *B. hermsii* and the OspC proteins of *B. burgdorferi*. When reading document D6, the skilled person would thus have identified the OspC proteins as a target to make vaccines against *B. burgdorferi* infection.

However, neither document D13 nor D6 suggested to look for other surface determinants. They did not provide

any sequence information which could have led to the nucleic acids or polypeptides of the invention.

Thus, the appellant's position as regards its objection of lack of inventive step was not convincing.

XIII. The appellant (opponent) requested that the decision under appeal be set aside and the patent be revoked.

XIV. The respondent (patent proprietor) requested that the patent be maintained on the basis of the sole request filed as auxiliary request 4 during the oral proceedings.

Reasons for the Decision

Compliance with the requirements of Articles 54, 83, 84 and 123 EPC

1. The appellant had no objections under Articles 54, 83, 84 and 123(2) EPC. The board is also satisfied that the request on file complies with the requirements of those articles.

Compliance with Article 56 EPC

2. In its statement of grounds, the appellant has relied upon two documents in support of its objection of lack of inventive step, namely documents D6 and D13, the latter being regarded by the appellant at the closest state of the art.

3. The respondent has challenged the admissibility of document D13 into the appeal proceedings, as being late filed evidence submitted only at the onset of the appeal proceedings. The board acknowledges that the only mention in passing of the bibliographic data of document D13 in two NCBI extracts, filed during the opposition proceedings as part of a compilation of such extracts and comparisons of sequences collectively named D4c, does not amount to a submission of document D13. The two afore-mentioned NCBI extracts provide indeed only the sequence of the Vmp11 and Vmp22 proteins of *Borrelia hermsii*, which have not been tested in the study of document D13. Admissibility of document D13 was not discussed at the oral proceedings of 16 December 2009 when the issue of inventive step was dealt with. Nevertheless, in view of the fact that the outcome of the assessment is in favour of the respondent, the board considers that it may rely on document D13 in the present decision.
4. Document D13 reports the discovery of a mechanism which permits *Borrelia hermsii*, a spirochete, that causes the arthropod-borne disease relapsing fever, to counter host immunity with multiphasic antigenic variation. In contrast to the two other known mechanisms generally described in the first and second full paragraphs in the right-hand column of page 867, which require DNA arrangements by means of an interplasmidic recombination or a pseudogene activation through an intramolecular deletion, the newly discovered mechanism produces amino changes through multiple postswitch point mutations of the expressed *vmp* gene (see in particular the first paragraph on the right-hand column

of page 868 and the first paragraph under the title "Discussion" on the left-hand column of page 872).

5. In view of that state of the art, the technical problem to be solved may be regarded as the identification of the genetic system which contributes to evasion of the immune response and long-term survival in the mammalian host upon infection by *Borrelia burgdorferi* and thereby the provision of proteins (and nucleic acid sequences encoding the same) for the diagnosis and the treatment of Lyme disease, the solution thereto being the nucleic acid sequence of claim 2 and a protein encoded thereby according to claim 1.
6. The question to be answered for the assessment of inventive step is whether a skilled person would have been in a position starting from document D13 in the light of document D6, the only other document relied upon by the appellant, to arrive at the proteins and nucleic sequences of claims 1 and 2.
7. Document D6 reports that some Vmps proteins of *Borrelia hermsii* belong together with OspC of *Borrelia burgdorferi* to a genus-wide family of 20 kDa proteins and that expression of these proteins may be coordinated with expression of other Vmp and Osp proteins in *Borrelia spp.* Thus, document D6 is referring to those membrane lipid proteins of *Borrelia burgdorferi* generally referred to as the Osp proteins which were known in the art at the relevant filing date (see paragraph 0007 on page 3 of the patent specification) and by no way suggests the existence of further outer membrane proteins, which, such as the Vmp

proteins of *Borrelia hermsii*, would be involved in a mechanism similar to those described in document D13.

8. In view of the additional fact that the study reported in document D13 concentrates on *B. hermsii* and does not contain any suggestion that a similar approach may be helpful to identify which genetic system may contribute to permit *Borrelia burgdorferi* to counter host immunity, the board considers that the skilled person attempting to combine the teachings of documents D13 and D6 would not have been in a position to identify and characterise the elaborate genetic system in the Lyme disease spirochete *Borrelia burgdorferi* that promotes extensive antigenic variation of the surface-exposed lipoprotein, named VlsE, identified by the inventors and found to be highly immunogenic (see paragraph 0269 on pages 40 and 41 of the patent specification).
9. The disclosure of the invention has made available to the public a new protein and proteins directly derivable therefrom (see claim 1) which, together with the corresponding encoding sequences (see claims 2 to 6) and a method of using the same to produce a polypeptide (see claim 7), constitute a valuable contribution to the art as it paves the way for a more reliable diagnosis and treatment of the Lyme disease with appropriate immunogenic polypeptides (see claims 8 to 9), protein compositions (see claims 10 to 12), antibodies (see claims 13 and 14), in vitro methods for the use of the same (see claims 15 and 16) and immunodetection kits (see claim 17).
10. Thus, the sole request on file as a whole involves an inventive step and thereby complies with Article 56 EPC.

Adaptation of the description

11. A number of amendments have to be carried out in order to adapt the description to the claims. Moreover, there are inappropriate references in Section 5.2 of the description (see paragraphs 0236 and 0237 on pages 35 and 36, respectively, of the patent specification) to Figures 8 to 11 which appear not to exist. For these reasons, the board considers that it is appropriate to remit the case to the first instance for adapting the description accordingly.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the first instance with the order to maintain the patent on the basis of the sole request filed as auxiliary request 4 during the oral proceedings, and a description and drawings to be adapted thereto.

The Registrar

The Chairman

A. Wolinski

L. Galligani