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D E C I S I O N
of 31 March 2004

Case Number: T 0839/01 - 3.3.8

Application Number: 89907985.9

Publication Number: 0419576

IPC: C12N 15/51

Language of the proceedings: EN

Title of invention:
Enterically transmitted non-A/non-B hepatitis viral agent

Applicant:
GENELABS TECHNOLOGIES, INC., et al

Opponent:
-

Headword:
Non-A/non-B hepatitis virus/GENELABS TECHNOLOGIES

Relevant legal provisions:
EPC Art. 83

Keyword:
"Sufficiency of disclosure - main request and auxiliary requests 1 to 11 (no)"

Decisions cited:
T 0694/02

Catchword:
-

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Case Number: T 0839/01 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 31 March 2004

Appellant: GENELABS TECHNOLOGIES, INC.
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 23 January 2001 refusing European application No. 89907985.9 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: F. L. Davison-Brunel
Members: M. R. Vega Laso
C. Rennie-Smith

Summary of Facts and Submissions

I. The present appeal lies from the decision of the examining division to refuse the European patent application No. 89 907 985, published as international application WO 89/12462 (EP A 0 419 576) with the title "Enterically transmitted non-A/non-B hepatitis viral agent", on the grounds that there was no text of the application agreed by the applicant and allowed by the examining division.

II. In the reasons for the decision the examining division stated that, in reply to its communication according to Rule 51(4) EPC in which the intention to grant a patent for the present application on the basis of the second auxiliary request filed during the oral proceedings held on 9 January 1996 had been expressed, the applicant had denied its approval to the text as intended for grant and filed instead a new request. The examining division had not consented to the amendments introduced by the new request under Article 86(3) EPC, arguing that they re-introduced subject-matter which had previously been objected to on the grounds of lack of clarity and lack of sufficient disclosure (Articles 83, 84 EPC), and had invited the applicant to comment on this issue or agree to the text proposed for grant. The applicant then requested a decision on the state of the file. The decision to refuse the application was issued on 23 January 2001.

III. On 29 March 2001 the applicant (appellant) lodged an appeal. A main request and three auxiliary requests were filed with the statement of grounds of appeal. As

a subsidiary request, oral proceedings according to Article 116 EPC were requested.

IV. In a communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal sent on 11 September 2003 with the summons to oral proceedings, the board stated that, in its provisional opinion, none of the sets of claims then on file fulfilled the requirements of Articles 83 and 84 EPC.

V. With a subsequent letter of 9 December 2003, the appellant filed a new main request and eleven auxiliary requests, of which auxiliary requests 6 to 11 differed from the main request and auxiliary requests 1 to 5 solely in that claim 21 had been deleted. The appellant announced that it would not be attending the scheduled oral proceedings, yet it did not withdraw its request therefor.

VI. Claim 1 of the **main request** and the **first, sixth and seventh auxiliary requests** read:

"1. A protein antigen which is immunoreactive with antibodies present in individuals infected with an enterically transmitted non-A/non-B viral hepatitis agent, which protein antigen is encoded by a nucleotide sequence comprising part of either

(a) the 1.33 kb DNA EcoRI insert present in plasmid pTZ-KF1 (ET1.1) carried in E.coli strain BB4 and having ATCC deposit no. 67717 or

(b) a nucleotide sequence which is able to hybridize with said insert and which has at most, 25-30%

base pair mismatches relative to said DNA EcoRI insert."

Claim 1 of the **second and eighth auxiliary requests** read:

"1. A protein antigen which is immunoreactive with antibodies present in individuals infected with an enterically transmitted non-A/non-B viral hepatitis agent, which protein antigen is encoded by either

(a) a nucleotide sequence comprising part of the 1.33 kb DNA EcoRI insert present in plasmid pTZ-KF1 (ET1.1) carried in E.coli strain BB4 and having ATCC deposit no. 67717 or

(b) a nucleotide sequence which is able to hybridize with said insert and which has at most, 25-30% base pair mismatches relative to said DNA EcoRI insert."

Claim 1 of the **third and ninth auxiliary requests** read:

"1. A protein antigen which is immunoreactive with antibodies present in individuals infected with an enterically transmitted non-A/non-B viral hepatitis agent, which protein antigen is encoded by either

(a) a nucleotide sequence comprising part of the 1.33 kb DNA EcoRI insert present in plasmid pTZ-KF1 (ET1.1) carried in E.coli strain BB4 and having ATCC deposit no. 67717 or

(b) a 100 to 300 base pair nucleotide sequence which is able to hybridize with said insert and which has at most, 25-30% base pair mismatches relative to said DNA EcoRI insert."

Claim 1 of the **fourth and tenth auxiliary requests** read:

"1. A protein antigen which is immunoreactive with antibodies present in individuals infected with an enterically transmitted non-A/non-B viral hepatitis agent, which protein antigen is encoded by a nucleotide sequence comprising part of either

(a) the 1.33 kb DNA EcoRI insert present in plasmid pTZ-KF1 (ET1.1) carried in E.coli strain BB4 and having ATCC deposit no. 67717;

(b) the nucleotide sequence <x>;

(c) the nucleotide sequence <z>;

or a sequence complementary to either said sequence (b) or (c)."

(<x> and <z> being DNA sequences described in the application as derived from viral strains isolated in Burma and Mexico, respectively, and corresponding to the 1.33 kb DNA insert, explanatory note by the board)

Claim 1 of the **fifth and eleventh auxiliary requests** read:

"1. A protein antigen which is immunoreactive with antibodies present in individuals infected with an

enterically transmitted non-A/non-B viral hepatitis agent, which protein antigen is encoded by a nucleotide sequence comprising part of either (a) the 1.33 kb DNA EcoRI insert present in plasmid pTZ-KF1 (ET1.1) carried in E.coli strain BB4 and having ATCC deposit no. 67717."

VII. The board decided to postpone oral proceedings, and in a further communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal, dated 22 January 2004, expressed serious doubts as to whether the new requests on file fulfilled the requirements of Articles 83 and 84 EPC.

VIII. In a fax letter received on 8 March 2004 the appellant reiterated that it did not intend to attend the re-scheduled oral proceedings.

IX. Oral proceedings took place in the absence of the appellant on 31 March 2004. At the end of the proceedings the board announced its decision.

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

In refusing the claims then on file under Article 83 EPC and/or Article 84 EPC, the examining division failed to take into account the full disclosure of the application as it would have been understood by the person skilled in the art, and in particular the contribution made to that art by the present invention.

The approach used by the applicant which resulted in the identification and characterisation of the enterically transmitted non-A/non-B hepatitis virus could be repeated. Alternatively, by using the 1.33 kb sequence disclosed in the application other cDNAs comprising sequences additional to that in the 1.33 kb fragment could be "fished" for, and these new fragments could be then used as probes to identify and sequence the entire viral genome. The genome of the ET-NANB hepatitis virus was only about 7.6 kb. Thus, the sequencing of the entire viral genome would not have been regarded as undue burden at the priority date.

ET-NANB hepatitis virus antigens could be obtained by putting the ET-NANB viral sequences, either disclosed in the application or obtained using the same as probes, in an expression system and screening the expression products with sera from infected patients.

The word "*comprising*" in the expression "*a nucleotide sequence comprising part of the 1.33 kb DNA EcoRI insert*" in the context of the claims did not lead to any ground of invalidity, was appropriate in providing commensurate protection and was not interpreted as laying a claim to the genome from which the 1.33 kb DNA EcoRI insert was isolated.

XI. The appellant claimed in its written submissions that it never intended to abandon the requests discussed and refused at the oral proceedings held on 9 January 1996, and that the failure by the examining division to give a reasoned written decision in respect of these requests amounted to a procedural violation. However,

it made no request for remittal of the case or for reimbursement of the appeal fee.

XII. The appellant requested in writing that the decision under appeal be set aside and a patent be granted on the basis of the main request or one of the eleven auxiliary requests filed with its letter of 9 December 2003.

Reasons for the Decision

1. The present application discloses the partial purification of an enterically transmitted non-A/non-B hepatitis virus (ET-NANB hepatitis virus) and provides the nucleotide sequence of a 1.33 kb fragment of the viral genome, this fragment being present as an insert in plasmid pTZ-KF1(ET1.1) carried in an *E. coli* strain deposited with the ATCC under deposit no. 67717. Also disclosed are corresponding partial viral genome sequences of other ET-NANB hepatitis virus strains considered to be related.

2. All requests on file have in common that their claim 1 covers the subject-matter of claim 1 of the fifth and eleventh auxiliary requests, namely a protein antigen which is immunoreactive with antibodies present in individuals infected with an enterically transmitted non-A/non-B viral hepatitis agent, which protein is encoded by a nucleotide sequence **comprising part of** the 1.33 kb DNA EcoRI insert present in plasmid pTZ-KF1(ET1.1) carried in *E. coli* strain BB4 and having ATCC deposit no. 67717.

3. In the board's judgement, the term "*comprising part of the 1.33 kb DNA EcoRI insert*" means "*containing at least part of the 1.33 kb DNA EcoRI insert or more*", which implies that "*the nucleotide sequence comprising part of*" may be the whole viral genome. In turn, this implies that protein antigens are claimed which may be encoded by any fragment of the whole genome, as long as somewhere on this fragment part of the 1.33 kb DNA is present, in addition to the coding sequence.

4. Thus, the claimed subject-matter concerns not only protein antigens encoded by the nucleotide sequence of the 1.33 kb DNA EcoRI insert explicitly disclosed in the application, but also protein antigens encoded by nucleotide sequences derived from the genome of the ET-NANB hepatitis virus but not disclosed in the application as filed. This has been admitted by the appellant (see paragraph X, above).

5. The question at issue is whether the latter subject-matter fulfils the requirements of Article 83 EPC, ie whether it is disclosed in the application as filed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

6. In the assessment as to whether a European application fulfils the requirements of Article 83 EPC, it is a well-established principle in the case law of the boards of appeal that, for the disclosure of an invention to be sufficiently clear and complete, the skilled person, on the basis of the information provided in the application itself and by using the common general knowledge at the application date (or the priority date, if applicable), has to be able to

achieve the desired result without undue burden (see eg decision T 694/92 OJ EPO 1997, 408).

7. The board notes that neither the virus, from which the 1.33 kb EcoRI insert is derived, nor the cDNA library containing other DNA fragments resulting from the reverse transcription of the viral RNA were deposited. For this reason, it is not possible to retrieve the whole specific ET-NANB hepatitis virus DNA starting with the 1.33 kb DNA as a probe and, consequently, the antigens encoded by this virus are also not reproducible. As for the antigens of other ET-NANB hepatitis virus strains which may eventually be isolated starting with the 1.33 kb fragment, they would not be expected to be identical to the antigens of the above mentioned specific virus, taking into account the known natural divergences between viral strains. For this reason alone, the requirements of Article 83 EPC are not fulfilled.

8. Furthermore, although not absolutely necessary for reaching a conclusion of lack of sufficiency in view of the above findings, it is worth mentioning that the very fact of producing immunogenic hepatitis viral antigens from viral strains yet to be isolated requires no less than eight steps:

(a) inoculate a cynomolgus monkey with a suspension from human stools positive for ET-NANB particles and confirm seroconversion to VLP("virus like particles")-positive serum (page 21, lines 2 to 30 of the application as filed);

(b) collect bile from the infected monkey, extract total RNA and synthesize cDNA from the extracted RNA (page 21, line 31 to page 22, line 4 of the application as filed);

(c) clone the cDNA fragments into a suitable cloning vector (eventually after fractionation of the cDNA fragments to obtain the desired size class) in order to obtain a cDNA library (page 22, lines 19 to 34 of the application as filed);

(d) screen the cDNA library for sequences specific for the ET-NANB hepatitis virus by differential hybridization to cDNA probes from infected and non-infected sources (page 22, line 35 to page 23, line 28 of the application as filed) or using the nucleotide sequence disclosed in the present application as probes;

(e) sequence the isolated cDNA fragments (page 23, line 30 to page 24, line 35 of the application as filed);

(f) confirm that the isolated cDNA fragments are in fact derived from a ET-NANB hepatitis virus, the genome of which contains a RNA sequence corresponding to the 1.33 kb DNA fragment;

(g) digest the isolated cDNA fragments and subclone shorter cDNA fragments containing open reading frames into an expression vector (section IV starting on page 28 of the application as filed); and

(h) assay the produced proteins/peptides for antigenicity using sera from infected and non-infected individuals.

9. A very substantial amount of work is, thus, required. Besides, the board has serious doubts that once a cloned cDNA has been identified according to step (c), it would be possible without undue burden to show that this cDNA originated from a virus the genome of which contains the 1.33 kb DNA fragment (step (f)), said cloned cDNA and the 1.33 kb fragment not necessarily being on the same molecule and the overall DNA content of the infected source not being easily determined.

10. The appellant's attention was drawn to these observations (paragraphs 7 to 9) in the communication sent with the summons to oral proceedings dated 11 September 2003 as well as in the communication dated 22 January 2004. In its answer (see paragraph X, above), the appellant failed to provide any reasons which would have enabled the board to re-consider the matter.

11. Thus, the board concludes that the requirements of Article 83 EPC are not met for the claimed subject-matter common to all requests on file.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski F. Davison-Brunel