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Datasheet for the decision of 24 February 2011

Case Number: T 1406/08 - 3.3.04

Application Number: 97932190.8

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Title of invention:
Cassava vein mosaic virus promoters and uses thereof

Applicant:
The Scripps Research Institute

Headword:
Cassava vein mosaic virus promoters/SCRIPPS

Relevant legal provisions:
EPC Art. 54, 56, 82, 83, 84, 123(2)

Keyword:
"Main request: added matter (no); unity, clarity, support, sufficiency of disclosure, novelty, inventive step (yes)"

Decisions cited:
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Catchword:
-

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Case Number: T 1406/08 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 24 February 2011

Appellant: The Scripps Research Institute
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 12 February 2008 refusing European patent application No. 97932190.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman: C. Rennie-Smith
Members: G. Alt
R. Gramaglia

Summary of Facts and Submissions

I. This is an appeal by the applicant (hereinafter "appellant") against the decision of the examining division refusing the European patent application No. 97 932 190.8. The application has the title "Cassava vein mosaic virus promoters and uses thereof". The application was filed on 20 June 1997 and claims the priority date of 20 June 1996.

II. The following documents are mentioned in this decision:

D1: Journal of General Virology, vol. 76, 1995, pages 1271-1276, Calvert, L.A. et al.

D2: Plant Molecular Biology, vol. 34, 1996, pages 1129-1139, Verdaguer, B. et al.

III. Hereinafter "Cassava vein mosaic virus" will be abbreviated as "CsVMV". An earlier abbreviation of CsVMV used in documents D1 and D2 is "CVMV".

IV. The decision under appeal deals with a single claim request. Its claim 1 reads:

"1. An isolated nucleic acid molecule comprising a promoter nucleotide sequence that is capable of initiating transcription of an operably linked heterologous nucleic acid sequence in a plant cell, wherein said promoter nucleotide sequence is selected from SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 and SEQ ID NO:17,

wherein the promoter sequence is separated from other portions of the CsVMV genome and the heterologous sequence is a non-CsVMV sequence."

Further claims related to vectors, transgenic plants and chimeric genes comprising the nucleotide sequence according to claim 1, and to a method of expressing a heterologous nucleic acid sequence comprising inter alia the step of transformation of a plant with the above-mentioned vector.

V. The examining division refused the application because the subject-matter of the claims lacked unity. One of the three inventions identified by the examining division, "[c]laimed invention 3" related to "[i]solated nucleic acid molecule comprising a promoter with SEQ ID Nos: 14-16, vectors, chimeric genes, transgenic plants and methods based on and in so far as they relate to said sequences" (see point 2.1.4 of the Reasons).

A further reason for refusal was lack of inventive step. The examining division was of the opinion that it was obvious in view of document D1 to arrive at the full-length promoter of CsVMV as represented by SEQ ID Nos. 1 and 2 and at its derivatives as represented by SEQ ID Nos. 4, 5, 9-13 and 17 (see in particular point 2.2.5 of the Reasons). No reasoning was given with respect to an inventive step of the subject-matter relating to SEQ ID Nos. 14 to 16 .

VI. With the statement of the grounds of appeal and with two further submissions in January and February 2011 the appellant filed several different claim requests.

VII. At the oral proceedings, which took place on 24 February 2011, the appellant filed a new main request which was the same as the "Fifth Auxiliary Request" and the "New Third Auxiliary Request" filed with the submissions of January and February, respectively. The new main request contained five independent claims, i.e. claims 1, 3, 4, 5 and 6 and one dependent claim, claim 2.

VIII. At the oral proceedings the board raised objections of lack of clarity with regard to terms and expressions in the new main request, namely "heterologous" and "operatively", used throughout the claims and "wherein the promoter sequence is separated from other portions of the CsVMV genome" and "that is heterologous with respect to the promoter, wherein the heterologous sequence is a non-CsVMV sequence" used in claims 1 and 6, respectively.

In reply to these objections the new main request was amended.

IX. Claims 1, 3, 4, 5, and 6 of the amended new main request (hereinafter "main request") read:

"1. An isolated nucleic acid molecule comprising a promoter nucleotide sequence that is capable of initiating transcription of an operably linked non-CsVMV nucleic acid sequence in a plant cell, wherein said promoter nucleotide sequence is selected from SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16, wherein the isolated nucleic acid molecule does not contain other portions of the CsVMV genome.

3. A vector comprising a promoter nucleotide sequence that is capable of initiating transcription of an operably linked non-CsVMV nucleic acid sequence in a plant cell, wherein said promoter nucleotide sequence is selected from SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16, and wherein said promoter nucleotide sequence is operably linked to a non-CsVMV nucleic acid sequence.

4. A transgenic plant comprising a promoter nucleotide sequence that is capable of initiating transcription of an operably linked non-CsVMV nucleic acid sequence in a plant cell, wherein said promoter nucleotide sequence is selected from SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16, and wherein said promoter nucleotide sequence is operably linked to a non-CsVMV nucleic acid sequence.

5. A method of expressing a non-CsVMV nucleic acid sequence in a plant cell comprising
a) transforming said plant cell with a vector according to claim 3; and
b) growing said plant cell under conditions where the non-CsVMV acid sequence is expressed in said plant.

6. A chimeric gene that expresses a non-CsVMV nucleic acid sequence in plant cells comprising operably linked in sequence in the 5' to 3' direction:
a) a promoter nucleotide sequence that is capable of initiating transcription of an operably linked non-CsVMV nucleic acid sequence in a plant cell, wherein said nucleotide sequence is selected from SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16, and

b) a structural nucleic acid sequence that is a non-CSVMV sequence."

X. The appellant submitted at the oral proceedings that the subject-matter of the amended claims had a basis in the application as filed and that the claims were clear.

With regard to the inventive step of the claimed subject-matter, the appellant argued inter alia as follows:

Document D2 was the closest prior art document. The problem to be solved was the provision of a promoter which was active in roots, but not, or only to a low level, in other tissues. The data for constructs pdDE1, pdDE2 and pdDE3 in Table 2 of the application provided evidence that the claimed subject-matter in fact solved the problem.

Document D2 disclosed in the first column on page 1138 elements from promoters of other pararetroviruses that conferred tissue-specific expression, namely in roots, vascular and leaf tissue. The document also disclosed that similar motifs were present in the CsVMV promoter. However, the skilled person would not be certain that these elements had in fact the predicted function in CsVMV. It was for example disclosed that the "root-motif" played a more complex role in the regulation of the promoter. Had the skilled person had no doubt about the role of any of the disclosed motifs for tissue-specific expression, he/she would have removed those motifs from the promoter conferring expression in vascular and leaf tissue in order to solve the problem underlying the application. However, the "leaf-motif"

was present in all of the claimed constructs. Thus, none of the claims was obvious in the light of document D2 and therefore all of them involved an inventive step.

XI. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the new main request filed at the oral proceedings.

XII. At the end of the oral proceedings the board announced its decision.

Reasons for the decision

1. The claims of the main request are amended with respect to the claims dealt with in the decision under appeal. Essentially, the claims are restricted to embodiments relating to SEQ ID Nos. 14 to 16. Moreover, the term "heterologous" is replaced by "non-CsVMV", the expression "wherein the promoter sequence is separated from other portions of the CsVMV genome" is replaced by the expression "wherein the isolated nucleic acid molecule does not contain other portions of the CsVMV genome", the term "operatively" is changed to "operably" and the definition in claim 6 "that is heterologous with respect to the promoter" is removed.

Article 123(2) EPC

2. The amended claims have a basis in the claims of the application as filed, referring explicitly to embodiments relating to SEQ ID Nos. 14, 15 and 16.

Furthermore, it is disclosed on page 13, lines 23 to 23 that the sequence which is linked to the promoter may be "from a source different from that from which the promoter was derived", i.e. that means that the sequence is a "non-CsVMV nucleic acid sequence" as now stated in the claims.

It is disclosed on page 14, lines 27 to 31 that the term "isolated nucleic acid" means that the nucleic acid does "not contain [...] the CsVMV promoter in the context of the CsVMV genome", i.e. this means that the isolated nucleic acid molecule does not contain other portions of the CsVMV genome.

Finally, it is disclosed on page 12, lines 15 to 18 that the terms "operably" and "operatively" have equivalent meaning.

3. Thus, the requirements of Article 123(2) EPC are fulfilled.

Article 84 EPC

4. The board does not see any ambiguity in the wording of the amended claims 1 to 6 of the main request. In particular, it is now clear that the nucleic acid linked to the promoter is "heterologous" with respect to the promoter and that CsVMV sequences other than the promoter sequences are absent.

5. Moreover, the subject-matter of the claims is amply supported by the disclosure in the description on for

example page 19, lines 20 to 26, page 23, line 1 to 22, page 25, lines 24 to 26, and page 32, lines 15 et seq.

6. Thus, the requirements of Article 84 EPC are fulfilled.

Article 83 EPC

7. The board considers that the disclosure in the application is sufficiently clear and complete as to enable the skilled person to carry out the claimed invention, in particular, because SEQ ID Nos. 14 to 16 are disclosed on pages 83 to 85. The examining division did also not raise an objection.

8. The requirements of Article 83 EPC are fulfilled.

Articles 54(1)(2) EPC

9. SEQ ID Nos. 14 to 16 are not disclosed in the priority document. Therefore the relevant date for determining the "state of the art" according to Article 54(2) is the filing date. Consequently, not only document D1, but also document D2 is prior art pursuant to Article 54(2) EPC. This is also the appellant's view.

10. SEQ ID Nos. 14 to 16 describe deletion variants of the full-length CsVMV promoter. Such variants are not disclosed in either of document D1 or D2. Consequently, the subject-matter of all claims - because they either relate to or refer to SEQ ID Nos. 14 to 16 - is novel. Also the examining division did not raise an objection in this respect.

11. The requirements of Article 54 EPC are fulfilled.

Articles 56 and 82 EPC

12. The present invention relates to variants of the CsVMV promoter which specifically drive expression in root tissue.

13. Of the only two documents available to the board, document D1 discloses the sequence of the CsVMV genome and points, inter alia, to the location of a TATA box - a well-known element of promoters. Document D2 discloses the sequence of the CsVMV promoter and inter alia that it is active in all organs of tobacco and rice plants, with particularly strong expression in vascular tissues, in leaf mesophyll cells and in the root tips (page 1137, first column). Thus, since it discloses the CsVMV promoter and its expression pattern, document D2 is the closest prior art document in relation to the claimed invention.

14. In view of document D2 the problem to be solved can be formulated as the provision of nucleic acid fragments having promoter activity in a restricted range of plant tissue, namely in roots.

15. The problem is solved according to claim 1 by nucleic acid fragments comprising the sequences set out in SEQ ID Nos. 14, 15 and 16.

16. According to the appellant the promoters denoted pdDE1, pdDE2 and pdDE3 correspond to SEQ ID Nos. 14 to 16 in Table 2 of the application. The data disclosed in the table for these constructs demonstrate that the promoters are active in root tips, and that they are

inactive or only weakly active in leaf mesophyll cells and phloem, i.e. vascular cells, respectively. Thus, the board is satisfied that the application provides evidence that the claimed subject-matter in fact solves the problem underlying the invention.

17. The claimed nucleic acid fragments are deletion variants of the full-length promoter disclosed in document D2, in particular of the fragment denoted CVP2 (see page 53, lines 13 to 15 and Figure 8 of the application). According to document D2 the fragment CVP2 extends from position -443 to +72 in the CsVMV genome with position 1 being the start site of transcription (document D2, the paragraph bridging pages 1132 and 1133).

18. According to Figure 8 and Table 2 of the application the deletions in the three constructs at issue are as follows:

(i) pdDE1 has a deletion from position -182 to position -63;

(ii) pdDE2 has a deletion from position -173 to position -63; and

(iii) pdDE3 has a deletion from position -149 to position -63.

19. In the assessment of the obviousness of the subject-matter of claim 1 the question to be answered is whether or not it was obvious for the skilled person to make these particular deletions in the sequence of the promoter disclosed in document D2 in order to transform

its tissue-non-specific activity into a root-specific activity.

20. Document D2 discloses motifs within the promoters of other pararetroviruses which are necessary for expression in particular tissues. Moreover, the document identifies similar motifs in the CsVMV promoter (page 1138, first column).

(i) A motif within the Cauliflower Mosaic Virus (CaMV) 35S promoter which "is able to confer expression principally in root tissues" is present at positions -203 to -219 of CsVMV.

(ii) A motif in the Commelina Yellow Mottle Virus (CoYMV) promoter located in a region "required for expression in vascular tissues" is correspondingly found at positions -90 to -111 in the CsVMV promoter.

(iii) A motif at positions -257 to -263 of the CsVMV promoter is identical with a motif in many other viral promoters and is the binding site for a leaf-specific nuclear factor. According to document D2 the presence of this motif in the CsVMV promoter could be the reason for the strong expression of genes from the CsVMV promoter in mesophyll cells.

21. The skilled person knows on the one hand that modifications in the sequence of a promoter, for example deletion of parts of it, may result in its complete inactivity. However, he/she also knows that promoter activity can be modified by appropriate sequence changes.

22. With this knowledge in mind, the skilled person, wanting to provide a root-specific variant of the ubiquitously active promoter disclosed in document D2, would be motivated by the disclosure in document D2 as cited above to prepare a promoter construct wherein (a) the portion suggested in document D2 to promote expression in root tissues is retained and wherein (b) the portions suggested to promote expression in leafs and vascular tissue are deleted. Thus, the skilled person would delete regions from the full-length CsVMV promoter matching more or less positions -90 to -111 and -257 to -263. At the same time, in order to avoid inactivation of the promoter, the skilled person would seek to keep the length of deletions to a minimum.

23. The deletions in the different constructs pdDE1, pdDE2 and pdDE3 concern positions -182 to -63, -173 to -63 and -149 to -63, respectively.

Thus, of the deletions that would be suggested to the skilled person by document D2, one is not present at all in any of claimed constructs, i.e. the deletion of -257 to -263. The other deletion is present, but is much larger than suggested which is surprising in view of the known danger to loose promoter activity.

24. The board concludes that document D2 cannot be considered as suggesting the deletions now present in the claimed constructs.

Hence, the subject-matter of claim 1 is not obvious in view of the disclosure in document D2.

25. The disclosure in document D1 does not allude to any elements in the genome of CsVMV that could confer tissue-specific, let alone root-specific expression.

Hence, the subject-matter of claim 1 is also not obvious in view of a combination of the disclosure in any of documents D1 and D2.

26. Claims 2 and 3 to 6 are either dependent on claim 1 or refer to SEQ ID Nos. 14 to 16 (see section IX above). Therefore, the conclusions drawn for claim 1 extend to these claims.

27. Thus, the subject-matter of the main request fulfils the requirements of Article 56 EPC.

28. It follows from the observations in points 13 to 15 above that the claimed subject-matter is linked so as to form a single general inventive concept. Hence the requirements of Article 82 EPC are fulfilled.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent on the basis of claims 1 to 6 of the new main request filed during the oral proceedings and a description and figures to be adapted thereto.

The Registrar: The Chairman:

P. Cremona C. Rennie-Smith