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Datasheet for the decision of 26 August 2014

Case Number: T 1639/09 - 3.3.02

Application Number: 02766144.6

Publication Number: 1421096

IPC: C07H21/02, A61K35/78, A01H1/00, A01H5/00

Language of the proceedings: EN

Title of invention:
CONSTITUTIVE PHOTOMORPHOGENESIS 1 (COP1) NUCLEIC ACID SEQUENCE FROM ZEA MAYS AND ITS USE THEREOF

Applicant:
Monsanto Technology LLC

Headword:
Zea mays COP1/MONSANTO

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no)

Decisions cited:
T 0386/94

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

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Case Number: T 1639/09 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 26 August 2014

Appellant: (Applicant)	Monsanto Technology LLC 800 North Lindbergh Boulevard St. Louis, Missouri 63167 (US)
Representative:	Von Kreisler Selting Werner - Partnerschaft von Patentanwälten und Rechtsanwälten mbB Deichmannhaus am Dom Bahnhofsvorplatz 1 50667 Köln (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 23 February 2009 refusing European patent application No. 02766144.6 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	U. Oswald
Members:	K. Giebeler
	L. Bühler

Summary of Facts and Submissions

I. European patent application No. 02 766 144.6, published as WO 03/020888 and entitled "Constitutive Photomorphogenesis 1 (COP1) nucleic acid sequence from *Zea mays* and its use thereof", was refused by decision of the examining division, pronounced on 13 January 2009 and dispatched on 23 February 2009, on the basis of Article 97(2) EPC for lack of an inventive step under Article 56 EPC.

II. Claim 1 of the sole request before the examining division, submitted with the applicant's letter dated 10 October 2007, reads as follows:

"An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide having an amino acid sequence that has at least 90% sequence identity to SEQ ID NO: 13 or a fragment thereof comprising an amino acid sequence that can bind to a native endogenous COP1 protein."

III. The documents cited during the examination and appeal proceedings include the following:

D3: WO 00/18940
D4: DNA Research (2001) 8, 73-79
D5: Mol. Genet. Genomics (2001) 265, 43-50
D15: Plant Cell (1993) 5, 729-737
D16: Plant Cell (2000) 12, 1307-1318
D17: Genome Biology (2002) 3, 1005.1-1005.6

IV. On inventive step, the examining division essentially argued as follows:

Starting from the closest prior art document D3, the technical problem to be solved was seen as the provision of the COP1 protein and nucleic acid from another plant to be used in the methods of document D3. The provision of the maize COP1 protein and nucleic acid would have been obvious to the skilled person in view of document D4 or D5, which described the identification of the rice COP1 cDNA by screening of a cDNA library using the known *Arabidopsis* COP1 cDNA as a probe. The skilled person would preferentially have selected rice COP1 cDNA as a probe for the identification of the maize COP1 cDNA. Numerous maize cDNA libraries had been available at the priority date of the present application. The knowledge of the whole genome of an organism was not a prerequisite for the identification of a cDNA in said organism. Moreover, documents D15 and D16 illustrated the usefulness of *Arabidopsis* sequences for isolating *Zea mays* orthologs.

V. The applicant (hereafter: appellant) lodged an appeal against this decision, maintaining the set of claims on which the examining division had decided.

VI. On 10 March 2014, the board summoned the appellant to oral proceedings.

VII. Oral proceedings before the board were held on 26 August 2014.

VIII. The appellant's arguments can be summarised as follows:

The claimed subject-matter involved an inventive step, because the skilled person would not have reasonably expected to succeed in the cloning of the maize COP1 gene when using probes based on the known *Arabidopsis* or rice COP1 gene. Documents D15 and D16 were not

relevant for the assessment of inventive step, because they reported the cloning of maize genes using *Arabidopsis* sequences which had a much higher effective sequence identity than that of maize and *Arabidopsis* COP1. But even if the screening was carried out, as suggested by the examining division, this would not lead to success due to the large differences between the *Arabidopsis* and maize COP1 sequences. The skilled person would furthermore not have known the number of genes and pseudo-genes that were similar to an isolated maize COP1 sequence, or the possible difficulties in determining which gene was the expressed gene and which expressed gene had the desired function. Moreover, it was known from document D17 that the *Arabidopsis* genome had limited value for maize genomics. Consequently, the skilled person would not have combined document D3 with documents D5/D6 and D15/D16.

The isolation of the maize COP1 gene had been a difficult task. The inventors had used the full-length *Arabidopsis* COP1 sequence to search a proprietary, non-public maize sequence (EST) database to identify a clone containing a fragment of the maize COP1 gene, and subsequent cloning was from a low abundance cDNA endosperm library. It was an additional obstacle that, at the filing date, the sequence of the maize genome, which was large and had complex genetic arrangements, had not yet been available.

There was furthermore no indication that it was possible to isolate the maize COP1 gene by using the rice COP1 gene as a probe; there would have been a great likelihood of failure.

Moreover, the maize COP1 sequence of the application was not merely an alternative to the known *Arabidopsis*

and rice sequences, but resulted in an unexpected and superior phenotype. The data presented in the grounds of appeal showed that transgenic maize plants expressing the fragment "ZmCOP1-N411", which comprised the protein dimerisation domain and sequences required for translocation from cytoplasm to nucleus, resulted in a significantly increased leaf area in mature plants and in a yield increase. By contrast, the prior art did not show any significant effect of the overexpression of COP1 sequences in mature plants and did not disclose any benefit of including sequences required for translocation from cytoplasm to nucleus in a COP1 fragment.

IX. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the single set of claims filed with letter dated 10 October 2007.

Reasons for the Decision

1. The appeal is admissible.

Inventive step (Article 56 EPC)

2. Claim 1 is directed to an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide having an amino acid sequence that has at least 90% sequence identity to SEQ ID NO: 13 or a fragment thereof comprising an amino acid sequence that can bind to a native endogenous COP1 protein.

The amino acid sequence of SEQ ID NO: 13 is the translated amino acid sequence of the full-length cDNA sequence of the maize Constitutive Photomorphogenesis 1

(COP1) gene (see the application, page 33, lines 21-24).

3. The closest prior art is document D3, which relates to producing plant cells and whole plants which contain a nucleic sequence coding for the wildtype COP1 gene as well as a nucleic acid sequence coding for the "Coil" domain of the COP1 protein (see abstract). These plants are described as displaying better emergence characteristics and improved seedling growth when grown under low light conditions (page 1, lines 11-13). The document further states that the nucleotide and amino acid sequences of COP1 had previously been provided from *Arabidopsis* (page 9, lines 8-10), pea (page 12, lines 1-2), spinach and rice (page 12, lines 8-10). Referring to document D6, document D3 reports that a COP1 homologue exists as a single copy gene in the rice genome and that the three structural domains of COP1 are highly conserved between *Arabidopsis* and rice (page 12, lines 14-16). The high degree of conservation between *Arabidopsis* and rice had been considered to be particularly interesting since the morphogenic development of monocotyledonous plants was different from that of dicotyledonous plants (page 12, lines 8-12). The document further states that "Considering the diversity of plant species in which a COP1 gene has been identified, the COP1 gene is most likely ubiquitous in the plant kingdom" (page 24, lines 2-3).

4. In view of this closest prior art, the technical problem to be solved is seen as the provision of a further nucleic acid molecule encoding a COP1-related protein.

4.1 The appellant has submitted that mature transgenic maize plants overexpressing a certain fragment of the

maize COP1 gene termed "ZmCOP1-N411", which encodes a polypeptide fragment containing the protein dimerisation domain and sequences required for the translocation from cytoplasm to nucleus, showed a surprising effect over the prior art. According to the appellant, the experimental data submitted with the grounds of appeal showed that the overexpression of the ZmCOP1-N411 fragment resulted in an improvement in the leaf width and yield of mature maize plants, whereas none of the cited prior art documents had disclosed any effect of overexpression of a COP1-related sequence on mature plants or had appreciated any potential advantages of the inclusion of sequences required for the translocation from cytoplasm to nucleus in a COP1 fragment to be used in an overexpression strategy.

The board notes that claim 1 is directed to a whole group of nucleic acid molecules, which group encompasses *inter alia* nucleic acid molecules encoding COP1-related polypeptide fragments which do not include sequences required for the translocation from cytoplasm to nucleus. Claim 1 thus encompasses nucleic acid molecules for which no unexpected effect has been alleged by the appellant. For this reason alone, the technical problem to be solved cannot be seen in the provision of a nucleic acid molecule encoding a COP1-related protein resulting in an improved plant phenotype. Hence the question whether or not the experimental data submitted by the appellant credibly show an advantageous effect of the ZmCOP1-N411 fragment is not relevant to the present decision.

5. The solution to the problem posed, as proposed by claim 1, is a group of nucleic acid molecules encoding polypeptides having an amino acid sequence relating to

the maize COP1 amino acid sequence and certain fragments thereof.

Having regard to Example 2 of the present application, the board is satisfied that the problem has indeed been solved.

6. The board considers that merely selecting maize COP1 did not involve an inventive step because, at the priority date, maize was commonly known as an economically important crop plant.

The key question to be asked when assessing inventive step of the subject-matter of claim 1 is thus whether, at the priority date, starting from the disclosure of document D3, the skilled person would have attempted the cloning of the maize COP1 gene with a reasonable expectation of success. Furthermore, it must be carefully considered whether the cloning of the maize COP1 gene involved unforeseeable difficulties which required inventive effort in order to solve them (see decision T 0386/94 of 11 January 1996, point 28).

7. At the priority date, the COP1 nucleic and amino acid sequences had been disclosed not only for the dicotyledonous plants *Arabidopsis*, pea and spinach, but also for the monocotyledonous plant rice. The COP1 gene was expected to be ubiquitous in the plant kingdom (see point 3 above). Therefore, the board is convinced that the skilled person would have assumed that a COP1 gene existed also in maize.

Furthermore, the high conservation of the three structural domains of COP1 (i.e. the Ring-finger domain, the Coil domain and the C-terminal WD-40 repeats domain) between the dicotyledonous plant

Arabidopsis and the monocotyledonous plant rice had been acknowledged in the prior art (see document D3, page 12, lines 14-16; page 9, lines 11-15). In view of this high conservation between the sequences from *Arabidopsis* and rice, the board is convinced that the skilled person would have expected an even higher conservation between rice and maize, which are both monocotyledonous plants and are commonly known to belong to the same botanical family (Poaceae, also called Gramineae), which means that they are more closely related than *Arabidopsis* and rice. Therefore, the board considers that, starting from the disclosure of document D3, the skilled person would have reasonably expected that the cloning of the maize gene could be achieved using the rice gene as a probe.

The board furthermore considers that this expectation would have been strengthened by document D6, which is referred to in document D3 and which describes in detail the isolation of the rice cDNA clone by homology screening of a rice cDNA library using the *Arabidopsis* COP1 cDNA as a probe.

In this situation, the board is convinced that the skilled person would have been highly confident that using the known rice cDNA in the screening of a maize cDNA library would result in the successful isolation of the maize cDNA.

7.1 The appellant submitted that the skilled person would not have had a reasonable expectation of success in obtaining the maize COP1 gene, since he/she would not have known the number of genes and pseudo-genes similar to an isolated maize COP1 sequence, or which difficulties would occur in determining which gene was

the expressed gene and which expressed gene had the desired function.

The board agrees that the skilled person would indeed not have had any certainty of obtaining the maize COP1 gene. However, the board is convinced that in view of the successful cloning of the rice gene using the *Arabidopsis* cDNA as reported in document D5, he/she would have been confident of successfully arriving at the cloning of the maize gene in a fairly straightforward manner.

7.2 The appellant further submitted that at the filing date the maize genome was, for the most part, exploratory and at a low redundancy. According to the appellant, the value of the maize genome sequence for the identification of maize genes was thus rather limited and there was no reasonable expectation of success in arriving at the claimed invention.

The board does not agree and takes the position that the fact that the sequence of the maize genome was not available at the priority date would not have affected the skilled person's expectation of success, because the knowledge of the whole genome of an organism is not necessary in order to arrive at the cloning of a gene, and numerous genes have been cloned before the complete genome of the organism in question was known.

8. Concerning the question of unforeseeable difficulties which required inventive effort in order to solve them, there is no evidence on file to indicate that any such difficulties would have occurred when using the rice cDNA as a probe for cloning the maize COP1 cDNA. The appellant's submission that there was a great likelihood of failure has not been substantiated by

evidence or convincing arguments. Moreover, the description of the present application confirms the high identity between the rice and maize sequences, which is stated to be 89% on the protein level (page 33, lines 27-32) and 77% or 71% on the nucleotide level (page 8, lines 4-6; page 33, lines 24-26). In this situation, the board concludes that the cloning of the maize COP1 gene, although requiring much work, did not pose such problems as to prove that the expectation of success was ill-founded.

8.1 The appellant has stressed that in order to arrive at the claimed invention, the inventors had used the full-length *Arabidopsis* COP1 sequence to search a proprietary non-public maize sequence (EST) database to identify a clone containing a fragment of the maize COP1 sequence, and that subsequent cloning was from a low abundance cDNA endosperm library, which made cloning difficult.

However, the board considers that by applying a cloning strategy using probes based on the known rice cDNA sequence, the cloning of the maize COP1 gene would have been possible without using the specific non-public maize EST database used by the inventors. Moreover, the board is convinced that the cloning of the maize COP1 gene would also have been possible without using the specific cDNA library used by the inventors, since document D4 describes the cloning of the rice COP1 gene from a root cDNA library, and document D5 describes the cloning of the rice COP1 gene from a green leaves cDNA library.

9. As concerns the further arguments presented by the appellant as to why the skilled person, in the light of documents D15 to D17, would not have reasonably

expected to be able to achieve the cloning of the maize COP1 gene using probes based on the available *Arabidopsis* sequence, the board need not comment on these arguments, since it is convinced that the skilled person would have reasonably expected, and been able, to achieve the cloning of the maize COP1 gene by using probes based on the known rice cDNA, without requiring inventive skill, as set out in point 8 above.

10. In view of the above, the board comes to the conclusion that the subject-matter of claim 1 does not involve an inventive step and that the sole request on file is not allowable under Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

N. Maslin U. Oswald

Decision electronically authenticated