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D E C I S I O N
of 16 October 2002

Case Number: W 0022/01 - 3.3.4

Application Number: PCT/US00/10247

Publication Number: WO 00/62620

IPC: A01N 63/00

Language of the proceedings: EN

Title of invention:
Transformed cells useful for the control of pests

Applicant:
University of Florida Research Foundation, Inc.

Opponent:
-

Headword:
Transformed cells/UNIVERSITY OF FLORIDA

Relevant legal provisions:
PCT Art. 17(3)(a), 34(3)(a)
PCT R. 40.1, 68.2, 13.1, 13.2, 13.3, 68.2, 68.3(c)

Keyword:
"Lack of unity a posteriori (groups 1 to 6) (no)"

Decisions cited:
G 0001/89, W 0013/87

Catchword:
-

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Case Number: W 0022/01 - 3.3.4
International Application No. PCT/US00/10247

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 16 October 2002

Applicant: University of Florida Research Foundation, Inc.

Representative: R.E. Perry
Gill JENNINGS & EVERY

Subject of the Decision: **Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fees) of the European Patent Office (International Preliminary Examining Authority) dated 11 April 2001.**

Composition of the Board:

Chairwoman: U. M. Kinkeldey
Members: R. E. Gramaglia
B. Günzel

Summary of Facts and Submissions

I. The Applicant filed International patent application PCT/US00/10247 on 18 April 2000. The application contained 77 claims of which claims 1, 2, 28, 61, 65, 70, 71 and 77 were as follows:

"1. A recombinant host transformed with a polynucleotide encoding a pesticidal polypeptide having at least one of the following three characteristics:

I) said polypeptide comprises a TMOF compound or a functional equivalent thereof, with the proviso that the polypeptide does not consist of $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$, $YDPAP_4$, NPTNLH or DF-OMe;

II) said polypeptide binds to a TMOF receptor or a functional equivalent thereof, with the proviso that the polypeptide does not comprise $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$, $YDPAP_4$, NPTNLH or DF-OMe and

III) said polypeptide comprises an NPF compound or a functional equivalent thereof.

2. The recombinant host, according to claim 1, wherein said polypeptide comprises an amino acid sequence having the general formula:

$$A^1A^2A^3A^4A^5F \qquad \text{(Formula I)}$$

wherein:

A^1 is selected from the group consisting of Y, A, D, F, G, M, P, S and Y;

A^2 is selected from the group consisting of A, D, E, F, G, N, P, S and Y;

A^3 is optionally present and is selected from the group consisting of A, D, F, G, L, P, S and Y;

A^4 is optionally present when A^3 is present and is selected from the group consisting of A, F, G, L and Y;

A^5 is optionally present when A^4 is present and is selected from the group consisting of A, F, L and P; and

F is a flanking region when is optionally present and is selected from the group consisting of: P, PP, PPP, PPPP, and PPPPP.

28. A method for controlling a pest wherein said method comprises applying to the pest, or to a pest-inhabited locus, a pesticidally effective amount of a composition comprising a recombinant host transformed with a polynucleotide encoding a pesticidal polypeptide having at least one of the following three characteristics:

[I)] said polypeptide comprises a TMOF compound or a functional equivalent thereof, with the proviso that the polypeptide does not comprise $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$, $YDPAP_4$, NPTNLH or DF-OMe;

II) said polypeptide binds to a TMOF receptor or a functional equivalent thereof, with the proviso that the polypeptide does not comprise $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$, $YDPAP_4$, NPTNLH or DF-OMe; and

III) said polypeptide comprises an NPF compound or a functional equivalent thereof.

61. A method for monitoring the presence of a transformed host in the environment wherein said method comprises providing a host which has been transformed with a polynucleotide sequence which encodes a flourescent compound, collecting an environmental sample in which the presence or absence of said transformed host is to be determined, and assaying said sample for the presence of said flourescent compound wherein the presence of said flourescent compound is indicative of the presence of said transformed host.

65. The method, according to claim 62, wherein said pesticidal polypeptide is selected from the group consisting of TMOF compounds, NPF compounds, and compounds which bind to a TMOF receptor.

70. A recombinant host which has been transformed to express a compound which fluoresces and a pesticidal polypeptide.

71. The recombinant host, according to claim 70, wherein said pesticidal polypeptide is selected from the group consisting of TMOF compounds, NPF compounds, and compounds which bind to a TMOF receptor.

77. A method for inhibiting the production of one or more digestive enzymes in a pest, comprising applying to the pest, or to a pest-inhabited locus, a pesticidally effective amount of a composition comprising a recombinant host transformed with a polynucleotide encoding a pesticidal polypeptide having at least one of the following three characteristics:

(a) said polypeptide comprises a TMOF compound or a functional equivalent thereof, with the proviso that the polypeptide does not comprise $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$ or $YDPAP_4$;

(b) said polypeptide binds to a TMOF receptor or a functional equivalent thereof, with the proviso that the polypeptide does not comprise $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$ or $YDPAP_4e$; and

(c) said polypeptide comprises an NPF compound or a functional equivalent thereof."

II. On 10 November 2000, the EPO, acting as International Searching Authority (ISA), issued to the Applicant an invitation to pay one additional search fee in accordance with Article 17(3)(a) and Rule 40.1 PCT because it considered that the international application covered two groups of inventions:

1. Claims: 21, 60, 68 and 75 completely and 1-18, 22-57, 61-66, 69-74 and 77 partially:

A recombinant host transformed with a pesticidal polypeptide comprising a TMOF (Trypsin Modulating Oostatic Factor) compound or a functional equivalent thereof; a transformed host, wherein said TMOF compound is selected from the group consisting of SEQ. ID. No. 4.

2. Claims: 19, 20, 58, 59, 67, 76 completely and 1-18, 22-57, 61-66, 69-74 and 77 partially:

A recombinant host transformed with a pesticidal polypeptide comprising a NPF (Neuropeptide F) compound or a functional equivalent thereof; a transformed host, wherein said NPF compound is selected from the group consisting of SEQ. ID. No. 1 and SEQ. ID. No. 2.

III. The Applicant did not pay the additional fee and the search was accordingly carried out for the first invention mentioned in the invitation by the ISA, namely that relating to TMOF-transformed hosts.

IV. On 22 February 2001, the EPO acting as International Preliminary Examining Authority (IPEA) issued to the Applicant an invitation as set forth in Article 34(3)(a) and Rule 68.2 PCT to restrict the claims or to pay 6 (six) additional examination fees because it considered that the subject-matter which had been searched did not comply with the requirement of unity of invention (Rule 13.1, 13.2 and 13.3 PCT). It indicated that this subject-matter related to seven inventions claimed in the following seven groups of claims:

1. Claims 1, 2, 12-14, 18, 21-29, 40, 44-57, 60, 62-66, 68-75 partially and claims 8, 9, 11, 35 and 38 complete: peptides comprising the amino acid sequence having the general formula A^1A^2 (A^1 and A^2 as defined in claim 2).

2. Claims 1, 2, 12-14, 18, 21-29, 40, 44-57, 60, 62-66, 68-75 and 77 partially and claims 6 and 10 complete: peptides comprising the amino acid sequence having the general formula $A^1A^2A^3$ (A^1, A^2 and A^3 as defined in claim 2).

3. Claims 1, 2, 12-14, 18, 21-29, 40, 44-57, 60, 62-66, 68-75 and 77 partially and claim 4 complete: peptides comprising the amino acid sequence having the general formula $A^1A^2A^3A^4$ (A^1, A^2, A^3 and A^4 as defined in claim 2).

4. Claims 1, 2, 12-14, 18, 21-29, 40, 44-57, 60, 62-66, 68-75 and 77 partially and claim 5 complete: peptides comprising the amino acid sequence having the general formula $A^1A^2A^3F$ (A^1, A^2, A^3 and F as defined in claim 2).

5. Claims 1, 2, 12-14, 18, 21-29, 40, 44-57, 60, 62-66, 68-75 and 77 partially and claim 7 complete: peptides comprising the amino acid sequence having the general formula A^1A^2F (A^1, A^2 and F as defined in claim 2).

6. Claims 1, 2, 12-14, 18, 21-29, 40, 44-57, 60, 62-66, 68-75 and 77 partially and claim 3 complete: peptides comprising the amino acid sequence having the general formula $A^1A^2A^3A^4F$ (A^1, A^2, A^3, A^4 and F as defined in claim 2).

7. Claim 61: method suitable for monitoring the presence of any transformed host.

V. As regarded claim groups 1 to 6 listed above, the IPEA argued that the common inventive concept underlying the claims could be seen in the provision of TMOF-derived fragments useful as pesticidal agents. However, since such fragments were already known from

(1) US-A-5,358,934 and

(2) US-A-5,130,253,

said common inventive concept no longer existed, in the absence of any further common technical feature which could be suitable to link the claimed subject-matter together as required by Rule 13.2 PCT.

VI. As for claim group 7 above, the IPEA argued that the method of claim 61 did not necessarily involve the use of a transformed host according to claim 1.

VII. With its response of 21 March 2001, the Applicant paid under protest five additional examination fees for the examination of the inventions identified as 1-6 by the IPEA and presented arguments that the inventions identified as 1 to 6 (see Section IV supra) were unitary.

VIII. With a communication dated 11 April 2001, a review board within the meaning of Rule 68.3(c) PCT confirmed the IPEA's opinion regarding lack of unity.

IX. On 11 May 2001 the Applicant paid the protest fee, filed new claims and presented further arguments that the inventions identified as 1 to 6 above were unitary. The Applicant requested reimbursement of the five additional examination fees, and of the protest fee.

Reasons for the Decision

1. The protest is admissible.

2. According to Rule 13.1 PCT, the international patent application shall relate to one invention only or to a group of inventions so linked as to form a single inventive concept. If the IPEA considers that the claims lack this unity, it is empowered, under Article 34(3) and Rule 68.2 PCT, to invite the Applicant to pay additional fees.

3. Lack of unity may be directly evident *a priori*, ie before the examination of the merits of the claims in comparison with the state of the art revealed by the search (cf., for example, decision W 13/87 of 9 August 1988). Alternatively, having regard to decision G 1/89 of the Enlarged Board of Appeal (EBA), dated 2 May 1990 (OJ EPO 1991, 155), the ISA is also empowered to raise an objection *a posteriori*, ie after having taken the prior art revealed by the search into closer consideration. This practice is laid down in the PCT Search Guidelines, Chapter VII,9 (PCT Gazette 30/1992, 14025) which are the basis for a uniform practice of all International Searching Authorities. The Enlarged Board of Appeal indicated that such consideration represents only a provisional opinion on novelty and inventive step which is in no way binding upon the authorities subsequently responsible for the substantive examination of the application (point 8.1. of the Reasons for the decision). In point 8.2 of the Reasons, the EBA mentioned that such invitation to pay additional fees should always be made "with a view to giving the Applicant fair treatment" and should only be made in clear cases. This approach, developed by the EBA in view of objections to unity of the invention issued by the ISA is equally applicable to objections to unity by the IPEA.

4. According to Rule 13.3 PCT, the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

5. The board firstly notes that with its submission dated 21 March 2001, the Applicant has not paid an additional fee for "invention 7" (see paragraph III supra), namely the method according to claim 61 for monitoring the presence of any transformed host. Therefore, the only

issue to be to dealt with by the board is whether or not inventions 1 to 6, for which the Applicant paid 5 (five) additional fees, are unitary.

6. The IPEA has based its finding of lack of unity upon a posteriori consideration. They found that "the common inventive concept underlying present claims can be seen in the provision of TMOF derived fragments useful as pesticidal agents. However, considering that such fragments are already taught in the prior art (see e.g. US-A-5,358,934 (1) and US-A-5,130,253 (2)) said common inventive concept no longer exists. Thus, in the absence of other technical features which would be suitable to link the claimed subject-matter together as required by Rule 13.2 PCT the subject-matter of present claims does not relate to one invention but to at least 7 separate ones".

7. However, in the board's judgement, the disclosure by documents (1) and (2) of TMOF-derived peptides has no effect upon the novelty of the claims at issue (referred to under Section II.1 supra), since they all relate to (or involve) **recombinant hosts** transformed with a polynucleotide encoding TMOF pesticidal polypeptides. None of these claims is indeed directed to TMOF polypeptides as such.

8. Therefore, the board disagrees to the finding by the IPEA that the technical problem solved by the claimed subject-matter lies with the provision of **TMOF-derived fragments** useful as pesticidal agents.

9. In order to define the underlying technical problem the closest state of the art has to be defined taking into account that the objected claims relate to **recombinant hosts** transformed with a polynucleotide encoding a TMOF pesticidal polypeptide.

10. Document (1) (see column 3, lines 26-31) discloses: "Bacteria, yeasts, and viruses each may be used to produce peptides for further use, or these hosts can be used as vehicles for direct application of the peptide to the target pest. Plants can be transformed so as to make the plant toxic to a target pest species which feeds on the plant". The "peptides" referred to in document (1) are: YDPAP, $YDPAP_2$, $YDPAP_3$ and $YDPAP_4$. Document (2), column 6, lines 58-63 discloses: "In application to the environment of the blood-ingesting insect the transformant strain will be applied to the natural habitat of the insect. The transformant strain will grow in the insect upon ingestion, while producing the peptide(s) which will have a deleterious effect on proteolytic enzymes biosynthesis and the ova". The "peptides" referred to in document (2) are: $YDPAP_6$, $DYPAP_6$, and PAP_6. Finally the passage of column 4, line 28 to column 5, line 43 of US-A-5,501,976 (document (3)), discloses $YDPAP_6$ and the application to the environment of the target pest of a transformant strain expressing this peptide. However, the disclosure of documents (1) to (3) in respect of the transformants merely constitutes theoretical considerations as to further possible uses of the particular peptides YDPAP, $YDPAP_2$, $YDPAP_3$, $YDPAP_4$, $YDPAP_6$, $DYPAP_6$, and PAP_6. Recombinant hosts containing either of the peptides mentioned above of documents (1) to (3) are disclaimed in the objected claims.

11. Therefore, these (now "disclaimed") recombinant hosts transformed with a polynucleotide encoding the TMOF pesticidal polypeptides $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$, $YDPAP_4$ as well as the method for the control of pest by administration to the pest of the transformed host expressing these pesticidal polypeptides must represent the closest prior art to the claimed subject-matter.

12. In the board's opinion, the technical problem to be solved vis-à-vis this closest prior art lies with the "reduction to practice" of the theoretical method hinted at by documents (1) to (3) for the control of pest by (possibly oral) administration to the pest of the transformed host expressing the pesticidal polypeptides $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$, $YDPAP_4$. This view is supported by Examples 2 and 3 of the application (see page 27), showing the successful application ("reduction to practice") of a method for controlling pest (here: mosquito larvae) by (orally) administering to the pest of transformed hosts expressing the pesticidal polypeptides $YDPAP_6$ (compare the XhoI-XbaI insert on page 28 with the "TMOF-gene" referred to in the Examples and in Fig. 8 to 10). The documents cited in the search report, though, either relate to the theoretical (ie non-experimentally verified) (oral or otherwise) administration to insects of transformed hosts expressing $YDPAP_6$, $DYPAP_6$, PAP_6, YDPAP, $YDPAP_2$, $YDPAP_3$ and $YDPAP_4$ (see point 10 supra) or to contacting the insect directly with a solution of the pesticidal peptide.

13. In order that the applicant be given "fair treatment" (see point 3 supra), the board does not exclude that this technical contribution (experimental demonstration that this way of administration via a recombinant host works) would not be relevant to the inventive step of the method of claim 28 at issue, and this cannot be considered a "clear case" as required by decision G 1/89 (see point 3 supra), having regard to the facts that:

Using as delivery vehicle a transformed cell expressing a TMOF peptide is prima facie something different from administering an excess of peptide directly to the insect. It has thus still to be debated whether the skilled person had a reasonable expectation of success

that the claimed delivery vehicle would have achieved sufficient concentrations of the (undegraded) TMOF peptide at the insect's gut receptor sites to inhibit trypsin biosynthesis and hence egg developement.

This view appears to be supported by the disclosure in the present application of particularly advantageous delivery vehicles such as eg the exemplified chlorella and yeasts (see page 25, line 18 to page 27, line 12).

14. But more importantly, the decisive question for the purpose of the present decision is the finding by the board that, contrary to the IPEA's conclusion, there **is** a "special technical feature that defines a contribution which each of the claimed inventions makes over the prior art" (see Rule 13.2 PCT).

15. As seen under point 12 supra the methods of claim 28 and dependent claims 29-57 and 60 contribute to putting into practice (and to experimentally demonstrate the feasibility of) the method of controlling a pest by applying to the pest a **recombinant host** transformed with a polynucleotide encoding a TMOF pesticidal polypeptide. Since claims 65-68 are addressed to methods of pest control by administration of transformed **recombinant hosts** encoding a TMOF-pesticidal polypeptide **and** a fluorescent compound, the fate of these claims follows that of claim 28. This also applies to the method of claim 77, also relying upon the administration to the pest of a **recombinant host** in order to inhibit the production of one or more digestive enzymes in the pest (the claim is merely an explanation of the mechanism by which the method of claim 28 works). Finally, the transformed **recombinant hosts** encoding a pesticidal polypeptide (claims 1-18 and 21-27) or encoding a pesticidal polypeptide **and** a fluorescent compound (claims 69-74) are means necessary and specifically designed for carrying out the pest

controlling method according to claims 28-57, 60, and 65-68. The fate of these claims is also tightly linked to that of claim 28 and related claims, which, as seen above, are unitary.

16. Therefore, the board cannot follow the IPEA's reasoning, according to which the searched subject-matter (inventions 1 to 6) is not considered as complying with the requirement of unity of invention. Hence, the invitation provided for in Article 34(3)(a) and Rule 68.2 PCT to pay 5 (five) additional search fees for inventions 1 to 6 cannot be regarded as legally effective, as it does not satisfy the requirement of Rule 40.1 PCT.

Order

For these reasons, it is decided that:

1. Refund of the 5 (five) additional examination fees paid by the Applicant is ordered.

2. The protest fee shall be refunded.

The Registrar: The Chairwoman:

P. Cremona U. M. Kinkeldey