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(84) Designated States (*regional*): European patent (AT, BE,  
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**Declarations under Rule 4.17:**

— *as to applicant's entitlement to apply for and be granted a  
patent (Rule 4.17(ii)) for the following designations AU, JP,  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,  
SI, SK, TR)*

— *as to the applicant's entitlement to claim the priority of the  
earlier application (Rule 4.17(iii)) for all designations*

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14 October 2004

**(15) Information about Correction:**

**Previous Correction:**

see PCT Gazette No. 28/2004 of 8 July 2004, Section II

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: MICROBIAL CONVERSION OF GLUCOSE TO PARA-HYDROXYSTYRENE

(57) Abstract: An *in vivo* method for the production of pHS via a recombinant host cell is disclosed. The host cell expresses at least one gene encoding a polypeptide having para-hydroxycinnamic acid decarboxylase activity in combination with either at least one gene encoding a polypeptide having tyrosine ammonia lyase activity or at least one gene encoding a polypeptide having phenylalanine ammonia lyase activity.

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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/17926

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C12N 9/88, 1/20, 15/00, 5/00, 5/02; C12P 21/06, 1/00; C07H 21/04; C07K 14/00  
 US CL : 435/232, 320.1, 325, 252.3, 410, 69.1, 41; 530/350; 536/23.2

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/232, 320.1, 325, 252.3, 410, 69.1, 41; 530/350; 536/23.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 WEST, MEDLINE, CAPLUS, BIOSIS, CABA, DGENE, PASCAL

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| A          | MOORE et al., Plant-like biosynthetic pathways in bacteria: from benzoic acid to chalcone, J. Nat. Prod., 2000, Vol. 65, pages 1956-1962.   | 1-14, 16-22           |
| A          | TAKEMOTO et al., Synthesis of styrenes through the biocatalytic decarboxylation of trans-cinnamic acids by plant cell cultures, Chem. Pharm. Bull., May 2001, Vol. 49, No. 5, pages 639-641.  | 1-14, 16-22           |
| A          | HASHIDOKO et al., Cloning of a DNA fragment carrying the 4-hydroxycinnamate decarboxylase (pofK) gene from Klebsiella oxytoca, and its constitutive expression in Escherichia coli JM109 Cells, Biosci. Biotech. Biochem., 1994, Vol. 58, No. 1, pages 217-218. | 1-14, 16-22           |
| A          | HWANG et al., Production of plant-specific flavanones by Escherichia coli containing an artificial gene cluster, Appl. Environ. Microbiol., May 2003, Vol. 69, No. 5, pages 2699-2706.  | 1-14, 16-22           |
| A          | HASHIDOKO et al., Induction of 4-hydroxycinnamate decarboxylase in Klebsiella oxytoca cells exposed to substrates and non-substrate 4-hydroxycinnamate analogs, Biosci. Biotechnol. Biochem., 2001, Vol. 65, No. 12, pages 2604-2612.                           | 1-14, 16-22           |

Further documents are listed in the continuation of Box C.  See patent family annex.

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|---|-----|--|
| * Special categories of cited documents:  | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "A" document defining the general state of the art which is not considered to be of particular relevance  | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "E" earlier application or patent published on or after the international filing date   | "Y" | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "&" | document member of the same patent family  |
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| "P" document published prior to the international filing date but later than the priority date claimed  |     |  |

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| Date of the actual completion of the international search<br>16 April 2004 (16.04.2004) | Date of mailing of the international search report<br><b>26 MAY 2004</b> |
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| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (703) 305-3230 | Authorized officer<br>Delia M. Ramirez <i>F. Roberts for</i><br>Telephone No. (571) 272-1600 |
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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/17926

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.: 15  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
There is no claim 15.
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
  4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest  The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.