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Published:
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PET FAMILY OF EFFLUX PROTEINS

(57) Abstract: The invention provides methods of increasing the production of aromatic carboxylic acids from a host cell via manipulation of the *yhcRQP* operon encoding a family of efflux proteins. Up-regulation of all or a sub-set of the genes in the *yhcRQP* were additionally found to enhance tolerance to aromatic carboxylic acids toxicity.

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INTERNATIONAL SEARCH REPORT

ernational application No.
PCT/US2004/001552

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

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

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 9,10,14
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:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 9,10,14

The specific sequence of claims 9, 10 and 14 have, according to PCT Rule 13ter.1c, not been searched since the Sequence Listing as present in the description does not comply with WIPO Standard ST 25 prescribed in the administrative instructions under Rule 5.2. The Sequence Listing has not been furnished in machine readable form as provided for in the same instructions and the applicant has not remedied the disclosed deficiencies within the time limit fixed in the invitation pursuant to PCT Rule 13ter.1.a.
Since claims 9, 10 and 14 rely on specific sequences (SEQ ID NO: 1-5) which were not available in computer-readable form, said claims could not be searched at all.
The subject-matter of the remaining claims 1-8, and 11-13 did not specifically refer to the sequences mentioned above but were restricted to the genes yhcQ and yhcP. However, said genes are not clearly defined as required from Article 6 PCT in order to allow a complete search. Without the specific sequence, the affected genes are defined merely by a name. However, said designation appears to be meaningless for a skilled person. A search with the specific names of the genes gives either no results or results pertaining to hypothetical genes/proteins with unknown function. The scope of the claims could thus not be limited by the use of the genes yhcQ and yhcP. Consequently, the search of claims 1-8 and 11-13 was restricted to a method of increasing the yield of aromatic carboxylic acids or increasing the resistance of a host cell to said aromatic carboxylic acids, wherein said host cells have an upregulated expression of genes encoding efflux/transporter proteins (but not yhcQ or yhcP).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/001552

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C51/00 C12N1/21

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)
IPC 7 C07C C12N

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 practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, FSTA, EMBASE, MEDLINE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LI XIAN-ZHI ET AL: "Role of the multidrug efflux systems of Pseudomonas aeruginosa in organic solvent tolerance" JOURNAL OF BACTERIOLOGY, vol. 180, no. 11, June 1998 (1998-06), pages 2987-2991, XP002296733 ISSN: 0021-9193 -----	
A	RAMOS JUAN L ET AL: "Efflux pumps involved in Toluene tolerance in Pseudomonas putida DOT-T1E" JOURNAL OF BACTERIOLOGY, vol. 180, no. 13, July 1998 (1998-07), pages 3323-3329, XP002296734 ISSN: 0021-9193 -----	

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[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"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)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"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

"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

"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.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 September 2004	21/10/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Bassias, I

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/001552

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RAMOS JUAN L ET AL: "Mechanisms of solvent tolerance in gram-negative bacteria." ANNUAL REVIEW OF MICROBIOLOGY. VOLUME 56 ANNUAL REVIEWS, 4139 EL CAMINO WAY, P. O. BOX 10139, PALO ALTO, CA, 94303-0139, USA SERIES : ANNUAL REVIEW OF MICROBIOLOGY (ISSN 0066-4227), 2002, pages 743-768, XP002296735 ISSN: 0-8243-1156-6	