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(71) Applicant *(for all designated States except US)*: **METABOLIC EXPLORER** [FR/FR]; Biopole Clermont-Limagne, F-63360 Saint Beauzire (FR).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **FIGGE, Rainer** [DE/FR]; 25 rue Marivaux, F-63200 Riom (FR). **SOUCAILLE, Philippe** [FR/FR]; Chant du Coucou, F-31450 Deyme (FR). **BARBIER, Guillaume** [FR/FR]; 8 rue d'Aline, F-63100 Clermont Ferrand (FR). **BESTEL-CORRE, Gwénaëlle** [FR/FR]; 3 Lotissement des Dômes, F-63360 Saint Beauzire (FR). **BOISART, Cédric** [FR/FR]; 15 rue Pierre Poisson, F-63400 Chamaliere (FR). **CHATEAU, Michel** [FR/FR]; Route de Marsat - les Beaumettes Bat E1, F-63200 Riom (FR).

(74) Agent: **CABINET REGIMBEAU - WARCOIN, AHNER, TEXIER, LE FORESTIER, CALLON DE LAMARCK, COLLIN, TETAZ**; 139 rue Vendôme, F-69477 Lyon Cedex 06 (FR).

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[Continued on next page]

(54) Title: INCREASING METHIONINE YIELD

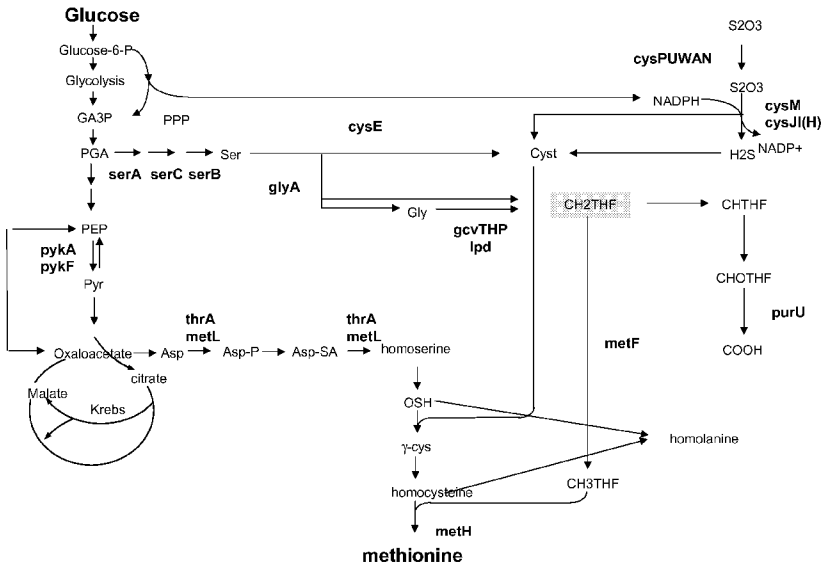

Fig. 1

(57) Abstract: Process for the production of methionine or its derivatives by culturing a microorganism in an appropriate culture medium comprising a source of carbon and a source of sulfur. The microorganism and/or the culture medium are modified in such way that the methionine/ carbon source yield is increased. The isolation of methionine or its derivates from the fermentation medium is also described.

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European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12P13/12

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)
C12P

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, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/020295 A (BASF AG [DE]; ZELDER OSKAR [DE]; HEROLD ANDREA [DE]; KLOPPROGGE CORINN) 22 February 2007 (2007-02-22) page 37, line 27 - page 38, line 1 page 247, line 15 page 53, line 5 - page 80, line 2 page 214, lines 4-19 page 237, line 12 - page 238, line 15 claims 5-22 ----- -/--	1,2,6, 9-20

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

[X] See patent family 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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 November 2008	23/04/2009

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, Fax: (+31-70) 340-3016	van de Kamp, Mart

INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KROMER ET AL: "Metabolic pathway analysis for rational design of L-methionine production by Escherichia coli and Corynebacterium glutamicum" METABOLIC ENGINEERING, vol. 8, no. 4, 1 July 2006 (2006-07-01), pages 353-369, XP005502384 ISSN: 1096-7176 the whole document page 360, right-hand column, line 9 - page 361, left-hand column, line 6 page 363, right-hand column, lines 11-13 page 368, left-hand column, lines 4-7	1,2,6, 9-20
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International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	the whole document 5. Media composition and culture conditions	4,5,7-19
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International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RAINER M FIGGE ED - VOLKER F WENDISCH: "Methionine Biosynthesis in Escherichia coli and Corynebacterium glutamiucum" MICROBIOLOGY MONOGRAPHS, SPRINGER-VERLAG, vol. 5, 1 January 2007 (2007-01-01), pages 163-193, XP008095720 ISSN: 1862-5576 [retrieved on 2006-12-09] the whole document	1,20
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2008/062859

Box No. 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.:
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:

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 No. 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:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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.:

1,5-7,9-20 (all partially); 2 and 4 (completely)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1,5-7,9-20 (all partially); 2 and 4 (completely)

A method for the production of methionine, comprising a step of culturing a modified microorganism in an appropriate culture medium, wherein compared to a non-modified microorganism the microorganism has been modified as in sub-invention 1.1, or wherein compared to a non-modified method the method has been modified as in sub-invention 1.2. A microorganism that has been modified as in sub-invention 1.1.

1.1. claims: 1,5-7,9-20 (all partially); 2 (completely)

A method for the production of methionine, comprising a step of culturing a modified microorganism in an appropriate culture medium, wherein compared to a non-modified microorganism the microorganism has been modified to present an enhanced methionine/carbon source yield by decreasing the deformylation of formyl-THF in the microorganism, by attenuation of the expression of the purU gene, possibly in combination with other modifications of the microorganism or the method. A microorganism that has been modified to present an enhanced methionine/carbon source yield by decreasing the deformylation of formyl-THF in the microorganism, by attenuation of the expression of the purU gene, possibly in combination with other modifications of the microorganism.

1.2. claims: 1,5,7-19 (all partially); 4 (completely)

A method for the production of methionine, comprising a step of culturing a modified microorganism in an appropriate culture medium, wherein compared to a non-modified method the method has been modified to present an enhanced methionine/carbon source yield by limiting growth and biomass production of the modified microorganism by limiting or starving the microorganism for one or several inorganic substrate(s) - eg phosphate and/or potassium - in the culture medium.

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2. claims: 1,5,6,8-20 (all partially); 3 (completely)

A method for the production of methionine, comprising a step of culturing a modified microorganism in an appropriate culture medium, wherein compared to a non-modified microorganism the microorganism has been modified to present an enhanced methionine/carbon source yield by decreasing the consumption of PEP in the microorganism, by attenuation of the expression of at least one of the pykA and pykF genes, possibly in combination with other modifications of the microorganism or the method. A microorganism that has been modified to present an enhanced methionine/carbon source yield by decreasing the consumption of PEP in the microorganism, by attenuation of the expression of at least one of the pykA and pykF genes, possibly in combination with other modifications of the microorganism.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2008/062859

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