

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(10) International Publication Number
WO 2017/149147 A3

(43) International Publication Date
08 September 2017 (08.09.2017)

(51) International Patent Classification:

C07K 14/435 (2006.01)

(21) International Application Number:

PCT/EP2017/055083

(22) International Filing Date:

03 March 2017 (03.03.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/303,973 04 March 2016 (04.03.2016) US

(71) Applicant: **EVOLVA SA** [CH/CH]; Duggingerstrasse 23,
CH-4153 Reinach (CH).

(72) Inventors: **HANSEN, Esben Halkjaer**; Howitzvej 20B
2, DK-2000 Frederiksberg (DK). **RASMUSSEN, Nina
Nicoline**; Glimvej 29, DK-2650 Hvidovre (DK). **NAES-
BY, Michael**; Stadthausgasse 18, CH-4051 Basel (CH).
DYEKJAER, Jane Dannow; J.A. Schwartz Gade 34, 2100
Copenhagen (DK). **CARLSEN, Simon**; Heimdalsgade 15,
2nd, 2200 Copenhagen (DK). **TAKOS, Adam Matthew**;
Lyshøjgårdsvej 85, 3 mf, 2500 Valby (DK). **OHLER,
Nicholas**; Duggingerstrasse 23, CH-4153 Reinach (CH).

(74) Agent: **SMAGGASGALE, Gillian Helen**; 138 Fetter
Lane, London EC4A 1BT (GB).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,
CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO,
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR,
KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:

28 December 2017 (28.12.2017)

(54) Title: PRODUCTION OF GIBBERELLINS IN RECOMBINANT HOSTS

(57) Abstract: The invention relates to recombinant microorganisms and methods for producing gibberellin compounds and gibberellin precursors.



WO 2017/149147 A3

INTERNATIONAL SEARCH REPORT

International application No PCT/EP2017/055083

A. CLASSIFICATION OF SUBJECT MATTER INV. C07K14/435 ADD.				
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) C07K				
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) EPO-Internal, BIOSIS, EMBASE, WPI Data				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	WO 02/055725 A2 (PHIBRO TECH INC DOING BUSINESS [US]) 18 July 2002 (2002-07-18) page 12 lines 24 to page 14 line 17; claims 40, 44, 45, 47-50, 52, 54, 55 -----	1,5-9, 11,14-41		
X	WO 2013/037959 A1 (VIB VZW [BE]; UNIV GENT [BE]; INZE DIRK GUSTAAF [BE]; DUBOIS MARIEKE []) 21 March 2013 (2013-03-21) page 2, lines 20-24; claims 4-8 page 5, lines 14-18 page 6, lines 7-10 -----	1,10, 14-20		
X	WO 2015/162283 A1 (EVOLVA SA [CH]) 29 October 2015 (2015-10-29) claims 1, 8, 9 paragraphs [0097], [0098], [0126], [0137] ----- -/--	1-5, 12-41		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.</td> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> See patent family annex.</td> </tr> </table>			<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> See patent family annex.
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> 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 application or patent 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			
13 November 2017	24/11/2017			
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Bladier, Cecile			

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/055083

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PETER HEDDEN ET AL: "Gibberellin biosynthesis and its regulation", BIOCHEMICAL JOURNAL, vol. 444, no. 1, 15 May 2012 (2012-05-15), pages 11-25, XP55380849, GB ISSN: 0264-6021, DOI: 10.1042/BJ20120245 the whole document</p> <p style="text-align: center;">-----</p>	<p>1-9,11, 14-41</p>
A	<p>A. BHATTACHARYA ET AL: "Characterization of the Fungal Gibberellin Desaturase as a 2-Oxoglutarate-Dependent Dioxygenase and Its Utilization for Enhancing Plant Growth", PLANT PHYSIOLOGY, vol. 160, no. 2, 21 August 2012 (2012-08-21), pages 837-845, XP55383780, Rockville, Md, USA ISSN: 0032-0889, DOI: 10.1104/pp.112.201756 the whole document</p> <p style="text-align: center;">-----</p>	<p>1-9,11, 14-41</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/055083

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 all searchable 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 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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 8, 9, 11(completely); 1-7, 14-41(partially)

-A recombinant host cell, comprising:

(a) a recombinant gene encoding a first cytochrome P450 polypeptide ; and

(b) a recombinant gene encoding a 2-oxoglutarate-dependent dioxygenase polypeptide and a second cytochrome P450 polypeptide ;

wherein the recombinant host cell is capable of producing a gibberellin precursor and/or a gibberellin compound.

-A method of producing a gibberellin precursor and/or a gibberellin compound in a cell culture, comprising growing said recombinant host cell in a cell culture, under conditions in which the genes are expressed;

wherein the gibberellin precursor and/or the gibberellin compound is produced by the recombinant host cell.

-A cell culture or a cell lysate comprising said recombinant host cell.

2. claims: 1-5, 14-41(all partially)

-A recombinant host cell, comprising:

(a) a recombinant gene encoding a first cytochrome P450 polypeptide ; and

(b) a second cytochrome P450 polypeptide ;

wherein the recombinant host cell is capable of producing a gibberellin precursor and/or a gibberellin compound.

-A method of producing a gibberellin precursor and/or a gibberellin compound in a cell culture, comprising growing said recombinant host cell in a cell culture, under conditions in which the genes are expressed;

wherein the gibberellin precursor and/or the gibberellin compound is produced by the recombinant host cell.

-A cell culture or a cell lysate comprising said recombinant host cell.

3. claims: 1, 5-7, 14-41(all partially)

-A recombinant host cell, comprising a recombinant gene encoding a 2-oxoglutarate-dependent dioxygenase polypeptide and a recombinant gene encoding a second cytochrome P450 polypeptide ;

wherein the recombinant host cell is capable of producing a gibberellin precursor and/or a gibberellin compound.

-A method of producing a gibberellin precursor and/or a gibberellin compound in a cell culture, comprising growing said recombinant host cell in a cell culture, under conditions in which the genes are expressed;

wherein the gibberellin precursor and/or the gibberellin compound is produced by the recombinant host cell.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

-A cell culture or a cell lysate comprising said recombinant host cell.

4. claims: 10, 12, 13(completely); 1, 5, 14-41(partially)

-A recombinant host cell, comprising a recombinant gene encoding a second cytochrome P450 polypeptide, wherein the recombinant host cell is capable of producing a gibberellin precursor and/or a gibberellin compound.

-A method of producing a gibberellin precursor and/or a gibberellin compound in a cell culture, comprising growing said recombinant host cell in a cell culture, under conditions in which the genes are expressed; wherein the gibberellin precursor and/or the gibberellin compound is produced by the recombinant host cell.

-A cell culture or a cell lysate comprising said recombinant host cell.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2017/055083

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02055725	A2	18-07-2002	
		AU 2002243235 A1	24-07-2002
		EP 1341926 A2	10-09-2003
		JP 2004517625 A	17-06-2004
		WO 02055725 A2	18-07-2002

WO 2013037959	A1	21-03-2013	
		US 2014344996 A1	20-11-2014
		WO 2013037959 A1	21-03-2013

WO 2015162283	A1	29-10-2015	
		EP 3134539 A1	01-03-2017
		US 2017044552 A1	16-02-2017
		WO 2015162283 A1	29-10-2015
