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(54) Title: GENES INVOLVED IN NOSCAPINE PRODUCTION

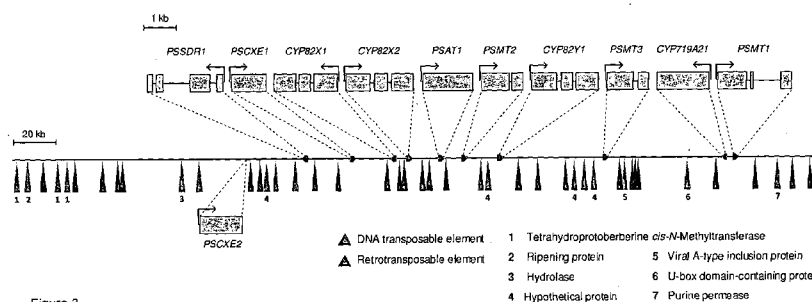


Figure 3

(57) Abstract: The disclosure relates to a nucleic acid molecule isolated from a *Papaver somniferum* cultivar that produces the opiate alkaloid noscapine which comprises 10 genes involved in the biosynthesis of opiate alkaloids.

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2013/050599

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/82 C07K14/415 A01H5/00
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)
C12N 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, CHEM ABS Data, BIOSIS, Sequence Search, 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 2012/010872 A2 (GLAXOSMITHKLINE AUSTRALIA PTY LTD [AU]; WINZER THILO [GB]; WALKER TRAC) 26 January 2012 (2012-01-26)	24-39, 41,42
Y	the whole document	1-23,40, 45,46
X	WO 2011/161431 A2 (GLAXOSMITHKLINE AUSTRALIA PTY LTD [AU]; WINZER THILO HANS [GB]; WALKER) 29 December 2011 (2011-12-29)	24-39, 41,42
Y	the whole document	1-23,40, 45,46
	----- -/-	



Further documents are listed in the continuation of Box C.



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

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10/09/2013

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2013/050599

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE UniProt [Online] 22 August 2006 (2006-08-22), "SubName: Full=CXE carboxylesterase; EC=3.1.1.1; Flags: Fragment;", XP002699426, retrieved from EBI accession no. UNIPROT:Q0ZPV6 Database accession no. Q0ZPV6 sequence -----	45,46
X	WO 02/101052 A2 (INST PFLANZENBIOCHEMIE [DE]; ZENK MEINHART H [DE]; KUTCHAN TONI M [DE]) 19 December 2002 (2002-12-19) the whole document -----	51
X	WO 99/14351 A1 (DU PONT [US]; FADER GARY MICHAEL [US]) 25 March 1999 (1999-03-25) the whole document -----	47,48
X	DATABASE UniProt [Online] 24 March 2009 (2009-03-24), "SubName: Full=Cinnamoyl-CoA reductase, putative; EC=1.1.1.219;", XP002711828, retrieved from EBI accession no. UNIPROT:B9SK36 Database accession no. B9SK36 sequence & AGNES P CHAN ET AL: "Draft genome sequence of the oilseed species Ricinus communis", NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US , vol. 28, no. 9 1 September 2010 (2010-09-01), pages 951-959, XP002676754, ISSN: 1087-0156, DOI: 10.1038/NBT.1674 Retrieved from the Internet: URL:http://www.nature.com/nbt/journal/v28/ n9/full/nbt.1674.html [retrieved on 2010-08-22] -----	51
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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2013/050599

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	J. M. HAGEL ET AL: "Quantitative 1H Nuclear Magnetic Resonance Metabolite Profiling as a Functional Genomics Platform to Investigate Alkaloid Biosynthesis in Opium Poppy", PLANT PHYSIOLOGY, vol. 147, no. 4, 1 August 2008 (2008-08-01), pages 1805-1821, XP055067990, ISSN: 0032-0889, DOI: 10.1104/pp.108.120493 -----	1-42, 45-48,51
A	CHAMPA P. WIJEKON ET AL: "Systematic knockdown of morphine pathway enzymes in opium poppy using virus-induced gene silencing", THE PLANT JOURNAL, vol. 69, no. 6, 28 December 2011 (2011-12-28), pages 1052-1063, XP055067993, ISSN: 0960-7412, DOI: 10.1111/j.1365-313X.2011.04855.x -----	1-42, 45-48,51
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A	HILEMAN L C ET AL: "Virus-induced gene silencing is an effective tool for assaying gene function in the basal eudicot species Papaver somniferum (opium poppy)", THE PLANT JOURNAL, BLACKWELL SCIENTIFIC PUBLICATIONS, OXFORD, GB, vol. 44, no. 2, 1 October 2005 (2005-10-01), pages 334-341, XP002689517, ISSN: 0960-7412, DOI: 10.1111/J.1365-313X.2005.02520.X [retrieved on 2005-08-26] ----- -/--	1-42, 45-48,51

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2013/050599

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DESGAGNÃ CR-PENIX ISABEL ET AL: "Integration of deep transcriptome and proteome analyses reveals the components of alkaloid metabolism in opium poppy cell cultures", BMC PLANT BIOLOGY, BIOMED CENTRAL, LONDON, GB, vol. 10, no. 1, 18 November 2010 (2010-11-18), page 252, XP021086707, ISSN: 1471-2229, DOI: 10.1186/1471-2229-10-252 -----	1-42, 45-48,51
A	B. FIELD ET AL: "Formation of plant metabolic gene clusters within dynamic chromosomal regions", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 108, no. 38, 20 September 2011 (2011-09-20), pages 16116-16121, XP055076488, ISSN: 0027-8424, DOI: 10.1073/pnas.1109273108 -----	1-42, 45-48,51
A	ADAM M. TAKOS ET AL: "Genomic clustering of cyanogenic glucoside biosynthetic genes aids their identification in Lotus japonicus and suggests the repeated evolution of this chemical defence pathway", THE PLANT JOURNAL, vol. 68, no. 2, 26 October 2011 (2011-10-26), pages 273-286, XP055076661, ISSN: 0960-7412, DOI: 10.1111/j.1365-313X.2011.04685.x -----	1-42, 45-48,51
A	KAZUNORI OKADA: "The Biosynthesis of Isoprenoids and the Mechanisms Regulating It in Plants", BIOSCIENCE, BIOTECHNOLOGY, AND BIOCHEMISTRY, vol. 75, no. 7, 1 January 2011 (2011-01-01), pages 1219-1225, XP055076663, ISSN: 0916-8451, DOI: 10.1271/bbb.110228 ----- -/--	1-42, 45-48,51

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2013/050599

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	T. WINZER ET AL: "A Papaver somniferum 10-Gene Cluster for Synthesis of the Anticancer Alkaloid Noscapine", SCIENCE, vol. 336, no. 6089, 31 May 2012 (2012-05-31), pages 1704-1708, XP055032027, ISSN: 0036-8075, DOI: 10.1126/science.1220757 the whole document -----	1-42, 45-48,51

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2013/050599

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.:

1-42, 45-48, 51
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: 1, 45, 46(completely); 3-42, 51(partially)

a carboxylesterase according to SEQ ID NO: 18 and
subject-matter relating thereto

2. claims: 2, 47, 48(completely); 3-42, 51(partially)

a short-chain dehydrogenase/reductase according to SEQ ID
NO: 19 and subject-matter relating thereto

3. claims: 43, 44(completely); 4, 16-23, 38, 40, 51(partially)

a cytochrome P450 according to SEQ ID NO: 17 and
subject-matter relating thereto

4. claims: 49, 50(completely); 4, 16-23, 38, 40, 51(partially)

an acetyltransferase according to SEQ ID NO: 20 and
subject-matter relating thereto

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2013/050599

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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WO 2009005647 A2	08-01-2009	NONE	