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— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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

Published:

— *with international search report (Art. 21(3))*

— *with sequence listing part of description (Rule 5.2(a))*

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17 April 2014

(54) Title: CELL CYCLE CONTROL FOR IMPROVING PROCESS PERFORMANCE AND RECOMBINANT EXPRESSION IN FUNGAL HOST CELLS

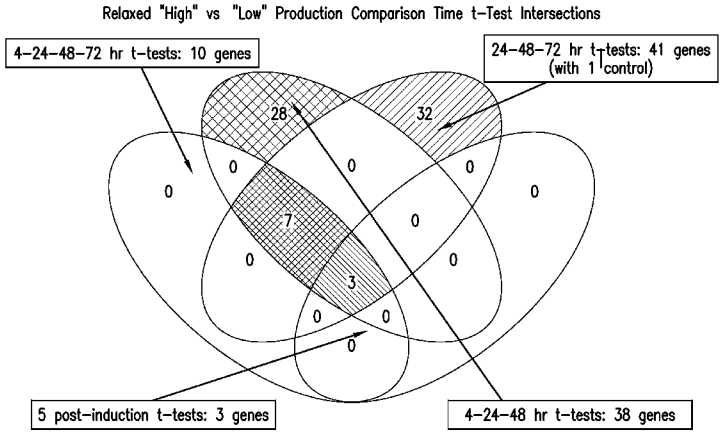

FIG.3

(57) Abstract: The present invention provides, in part, isolated host cells that overexpress various cell cycle control genes which exhibit robust levels of protein expression and secretion. Methods for expressing proteins with the cells and for identifying such cells are also provided.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/24116

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12P 21/06 (2012.01)
USPC - 435/69.1; 435/254.23
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)
USPC: 435/69.1; 435/254.23

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 435/69.1, 254.23, 254.2 (text search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Electronic data bases: PubWEST (USPT, EPAB, JPAB, PGPB); Google Scholar, GenCore sequence search (NT)
Search terms: Pichia pastoris, fungus, yeast, Saccharomyces cerevisiae, cell cycle, CYB2, CLB2, CLB4, CLN3, CLN4, CDC28, homologue, overexpression, heterologous protein, yield, production, secretion

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	UCHIYAMA et al., Cell cycle dependency of rice alpha-amylase production in a recombinant yeast. Biotechnol Bioeng, 5 May 1997, Vol 54, No 3, Pages 262-271. Especially abstract, pg 263 col 2 para 2, pg 269 col 2 para 1, pg 270 col 1 para 1.	1-6
Y	CROSS et al., Quantitative characterization of a mitotic cyclin threshold regulating exit from mitosis. Mol Bio Cell, May 2005, Vol 16, No 5, Pages 2129-2138. Especially abstract, pg 2131 col 1 para 1.	1-6
Y	GenBank FN392320. Pichia pastoris GS115 chromosome 2, complete sequence, 8 July 2009 [online]. [Retrieved 2 May 2012]. Retrieved from the internet: <URL: http://www.ncbi.nlm.nih.gov/nucleotide/238030677?report=gbwithparts&from=187101&to=188309&RID=UN9AMKC1016>. Especially pg 2.	2
A	GenBank NM_001184216.1. Saccharomyces cerevisiae S288c Clb2p (CLB2) mRNA, complete cds, 17 August 2010 [online]. [Retrieved on 2 May 2012]. Retrieved from the internet: <URL: http://www.ncbi.nlm.nih.gov/nuccore/296148757?sat=14&satkey=6231181>. Especially pg 2.	1-6
A	DE SCHUTTER et al.Genome sequence of the recombinant protein production host Pichia pastoris. Nature Biotechnol June 2009, Vol 27, No 6, Pages 561-566. Especially abstract.	1-6

☒ Further documents are listed in the continuation of Box C. ☐

* 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)
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"P" document published prior to the international filing date but later than the priority date claimed
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"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
2 May 2012 (02.05.2012)	07 JUN 2012
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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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,P	WO 2012/004226 A1 (MATTANOVICH et al.) 12 January 2012 (12.01.2012). Especially pg 4 ln 30 continued to pg 6 ln 5.	1-6
X,P	BUCHETICS et al., Reverse engineering of protein secretion by uncoupling of cell cycle phases from growth. Biotechnol Bioeng ePub 6 May 2011, Vol 103, Pages 2403-2412. Especially abstract.	1-6
A	US 2010/0297738 A1 (GASSER et al.) 25 November 2010 (25.11.2010). Especially para [0044 -0064].	1-6