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IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent
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TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM,
ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA,
SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
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(54) Title: METHOD TO INCREASE PROTEIN PRODUCTION IN CULTURE

(57) Abstract: A new recombinant protein production methodology has been discovered for expression of genes of interest. This should be useful for low or poorly expressing genes and in cellular production of high levels of proteins when such high levels may be detrimental or stressful to cells. Isolated polynucleotides encoding a spliced form XBP-1, ATF6, and eIF2 α S51A are disclosed. Expression vectors comprising these polynucleotides are useful in increasing the specific cellular productivity in a cell expressing a polypeptide of interest by augmenting the unfolded protein response in a cell. Finally, methods to increase specific cellular productivity in mammalian cells using the above mentioned polynucleotides are also disclosed.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
 IPC(7) : C12N 5/00, 15/00, 15/63; C12P 21/06; C12Q 1/68; G01N 33/567
 US CL : 435/455, 69.1, 375, 325, 320.1, 6, 7.21
 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)
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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)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT ...

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	YOSHIDA et al, XBP1 mRNA Is Induced by ATF6 and Spliced by IRE1 in Response to ER Stress to Produce a Highly Active Transcription Factor, Cell, 2001, Vol. 17, pages 881-891, see e.g. page 890 and page 885.	1-5, 9, 22, 23, 26, 28, 29, 34, 40-42, 44, 46, 48 and 60
Y	WU et al, Ultraviolet Light Inhibits Translation through Activation of the Unfolded Protein in Response to Kinase PERK in the Lumen of the Endoplasmic Reticulum, JBC, 2002, Vol 277, No. 20, pages 18077-18083, see especially page 18080.	13 and 38
Y	PEAKMAN et al, Comparison of expression of a humanized monoclonal antibody in mouse NSO myeloma cells and Chinese Hamster Ovary cells, Human Antibodies Hybridomas, 1994, Vol. 5, No. 1 and 2, pages 65-74, see especially page 68.	6, 15-21, 25, 27, 45, 47, 49-59
X	SHUDA et al, Activation of the ATF6, XBP1 and grp78 genes in human hepatocellular carcinoma: a possible involvement of the ER stress pathway in hepatocarcinogenesis, J Hepatology, 2003, Vol. 38, pages 605-614, see entire document.	1-4, 9-11, 22, 23 and 26

Further documents are listed in the continuation of Box C. See patent family annex.

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

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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.
Y	SUGUIRA, T. Baculoviral expression of correctly processed ADAMTS proteins fused with the human IgG-Fc region, J Biotechnology, 2002, Vol 100, pages 193-201, see entire document.	24 and 43

INTERNATIONAL SEARCH REPORT

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Continuation of B. FIELDS SEARCHED Item 3:
EAST databases- USPAT, PGPUB, EPO, JPO, Derwent, IBM-IDB
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