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(54) Title: METHODS FOR PRODUCING MODIFIED GLYCOPROTEINS

(57) Abstract: Cell lines having genetically modified glycosylation pathways that allow them to carry out a sequence of enzymatic reactions, which mimic the processing of glycoproteins in humans, have been developed. Recombinant proteins expressed in these engineered hosts yield glycoproteins more similar, if not substantially identical to their human counterparts. The lower eukaryotes, which ordinarily produce high-mannose containing *N*-glycans, including unicellular and multicellular fungi are modified to produce *N*-glycans such as Man<sub>5</sub>GlcNAc<sub>2</sub> or other structures along human glycosylation pathways. This is achieved using a combination of engineering and/or selection of strains which: do not express certain enzymes which create the undesirable complex structures characteristic of the fungal glycoproteins, which express exogenous enzymes selected either to have optimal activity under the conditions present in the fungi where activity is desired, or which are targeted to an organelle where optimal activity is achieved, and combinations thereof wherein the genetically engineered eukaryote expresses multiple exogenous enzymes required to produce "human-like" glycoproteins.

## INTERNATIONAL SEARCH REPORT

 Internat Application No  
 PCT/US 01/20553

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C12P21/00 C12N1/14 C12N9/24 C12N9/10 C12N5/10 C12N15/62 //C12R1/645		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12P C12N		
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, BIOSIS, MEDLINE, WPI Data, PAJ		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHIBA YASUNORI ET AL: "Production of human compatible high mannose-type (Man5GlcNAc2) sugar chains in Saccharomyces cerevisiae." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 41, 9 October 1998 (1998-10-09), pages 26298-26304, XP002202331 ISSN: 0021-9258 Figure 1 the whole document --- -/--	1-34
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in 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 *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  25 June 2002		Date of mailing of the international search report  12/07/2002
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  Aslund, J

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
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**INTERNATIONAL SEARCH REPORT**  
 Information on patent family members

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