



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

<p>(51) International Patent Classification<sup>6</sup> : <b>C12N 15/81, C12P 21/02</b></p>	<p><b>A3</b></p>	<p>(11) International Publication Number: <b>WO 99/37758</b> (43) International Publication Date: 29 July 1999 (29.07.99)</p>
<p>(21) International Application Number: PCT/US99/01627 (22) International Filing Date: 27 January 1999 (27.01.99) (30) Priority Data: 60/072,691 27 January 1998 (27.01.98) US (71) Applicant: THE BOARD OF REGENTS OF THE UNIVERSITY AND COMMUNITY COLLEGE SYSTEM OF NEVADA on behalf of THE UNIVERSITY OF NEVADA-RENO [US/US]; University of Nevada-Reno, Reno, NV 89557 (US). (72) Inventors: COURCHESNE, William, E.; 7300 Cascade Road, P.O. Box 1058, Soda Springs, CA 95728 (US). SCHOLEY, David, A.; 10 Irving Park Circle, Reno, NV 89503 (US). COPLEY, Kathrin; 11022 Portobelo Drive, San Diego, CA 92124 (US). (74) Agent: ADLER, Reid, G.; Morgan, Lewis &amp; Bockius LLP, 1800 M Street, N.W., Washington, DC 20036-5869 (US).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 30 September 1999 (30.09.99)</p>	
<p>(54) Title: EXPRESSION OF PROTEOLYTICALLY-SENSITIVE PEPTIDES</p>		
<p>(57) Abstract</p> <p>Compositions and methods are disclosed for the production of polypeptides sensitive to proteolysis due to their content of arginine and lysine residues. The methods of the invention utilize yeast cells with reduced expression of either or both of the proteases encoded by <i>YAP3</i> and <i>MKC7</i>. The methods of the invention also utilize yeast cells with reduced activity for either or both of the <i>Yap3</i> and <i>Mkc7</i> proteases. While a yeast expression system is used to demonstrate the invention, any eukaryotic cell which normally has homologues to the <i>Yap3</i> and <i>Mkc7</i> endoproteases may be used in the disclosed compositions and methods.</p>		

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/01627

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 6 C12N15/81 C12P21/02

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)

IPC 6 C12N C12P

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)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 01473 A (NOVO-NORDISK A/S) 15 January 1998 (1998-01-15) * pages 1-9; claims * ---	1-20
X	WO 98 01535 A (NOVO-NORDISK A/S) 15 January 1998 (1998-01-15) * pages 1-10; claims * ---	1-20
X	WO 95 23857 A (DELTA BIOTECHNOLOGY LIMITED) 8 September 1995 (1995-09-08) * pages 1-10; claims * ---	1-20
A	EP 0 327 797 A (BOEHRINGER MANNHEIM GMBH) 16 August 1989 (1989-08-16) * pages 1-4 * -----	1-20

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Patent family members are listed in annex.

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# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 99/01627

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9801473    A	15-01-1998	AU    3255397 A	02-02-1998
WO 9801535    A	15-01-1998	AU    3255497 A CA    2258307 A EP    0909312 A	02-02-1998 15-01-1998 21-04-1999
WO 9523857    A	08-09-1995	AU    683728 B AU    1818395 A CA    2183241 A EP    0749478 A GB    2301365 A,B JP    9509581 T	20-11-1997 18-09-1995 08-09-1995 27-12-1996 04-12-1996 30-09-1997
EP 0327797    A	16-08-1989	DE    3804890 A JP    2002385 A US    5179003 A	13-07-1989 08-01-1990 12-01-1993