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(21) International Application Number: PCT/US92/11188 (22) International Filing Date: 23 December 1992 (23.12.92) (30) Priority data: 07/813,324 24 December 1991 (24.12.91) US 07/876,680 30 April 1992 (30.04.92) US (71) Applicant: GENZYME CORPORATION [US/US]; One Kendall Square, Cambridge, MA 02139-1562 (US). (72) Inventors: BARNGROVER, Debra, A. ; 163 Cochituate Road, Wayland, MA 01778 (US). MCPHERSON, John ; 31 Valleywood Road, Hopkinton, MA (US). (74) Agents: ARNOLD, Beth, E. et al.; Genzyme Corporation, One Kendall Square, Cambridge, MA 02139 1562 (US).		(81) Designated States: CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 28 October 1993 (28.10.93)
(54) Title: METHOD FOR INCREASING RECOMBINANT PROTEIN PRODUCTION (57) Abstract Methods and compositions for increasing the production of recombinant proteins are provided. In one aspect, eukaryotic expression systems are cultured in media containing an appropriate amount of transforming growth factor- β . In another aspect, eukaryotic expression systems are cultured in glutamate-containing, essentially glutamine-free media.		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 92/11188

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int.Cl. 5 C12P21/02; C12N9/24; C12N5/00; //C12N5/10 C12N15/56		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int.Cl. 5	C12N ; C07K	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ^o	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
Y	WO,A,9 007 573 (GENZYME CORPORATION) 12 July 1990 see the whole document ---	1-16
Y	JOURNAL OF DERMATOLOGY vol. 18, no. 5, May 1991, TOKYO, JP pages 252 - 257 HASHIRO, M. ET AL. 'Stimulation of fibronectin secretion in cultured human keratinocytes by transforming growth factor-beta not by other growth inhibitory substances' see the whole document ---	1-8
Y	WO,A,9 003 430 (CETUS CORPORATION) 5 April 1990 see page 8, line 3 - line 28	9-16
A	see claim 11 ---	1
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IV. CERTIFICATION		
Date of the Actual Completion of the International Search 03 SEPTEMBER 1993		Date of Mailing of this International Search Report 23 -09- 1993
International Searching Authority EUROPEAN PATENT OFFICE		Signature of Authorized Officer ANDRES S.M.

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	CLINICAL RESEARCH vol. 35, no. 3, April 1987, page 725A WIKNER, N.E. ET AL. 'Transforming growth factor-beta stimulates the expression of fibronectin by human keratinocytes' see left column, 2nd abstract ---	1-8
A	BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS vol. 138, no. 2, 31 July 1986, DULUTH, MINNESOTA US pages 974 - 980 VARGA, J. & JIMENEZ, S.A. 'Stimulation of normal human fibroblast collagen production and processing by transforming growth factor-beta' see the whole document ---	1-8
A	ABSTRACTS OF PAPERS OF THE 196th NATIONAL MEETING OF THE AMERICAN CHEMICAL SOCIETY; LOS ANGELES, CALIFORNIA; September 25-30, 1988; Abstract MBTD 141; FIELD, R.P.: 'Suspension growth of recombinant CHO cells in serum-free and glutamine-free medium' see abstract ---	9-16
A	EP,A,0 307 247 (GENENTECH, INC.) 15 March 1989 see 'Detailed Description' -----	1-8

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

US 9211188
SA 68862

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on
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03/09/93

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