

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
25 May 2001 (25.05.2001)

PCT

(10) International Publication Number
WO 01/36640 A3

- (51) International Patent Classification⁷: C12N 15/12, C07K 14/50, C12N 5/10, C07K 16/22, A61K 38/18
- (74) Agents: POTTER, Jane, E.; SEED Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 et al. (US).
- (21) International Application Number: PCT/US00/31745
- (22) International Filing Date: 16 November 2000 (16.11.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/166,540 18 November 1999 (18.11.1999) US
60/203,633 11 May 2000 (11.05.2000) US
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, 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, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, 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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- (71) Applicants: CHIRON CORPORATION [US/US]; 4560 Horton Street, Emeryville, CA 94608 (US). KYOTO UNIVERSITY [JP/JP]; Yoshida-Shimoadachi, Sakyo, Kyoto 606-8501 (JP).
- (72) Inventors: ITOH, Nobuyuki; Yoshida-Shimoadachi, Sakyo, Kyoto 606-8501 (JP). KAVANAUGH, W., Michael; 4560 Horton Street, Emeryville, CA 94608 (US).
- Published:
— with international search report
- (88) Date of publication of the international search report:
11 October 2001

[Continued on next page]

(54) Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PRODUCTS

```

human FGF-21      MDSDETGF EHSGLWVSLAGLLLGACQAHPIPDSSPLLQFG-GQV-RQRYLYTD      52
                  ** * * * * * * ** * * * ***
mouse FGF-15     MARKWNGRAVARALVLATLWLAVS-GRPLAQ-QSQSVSDEDPLFLYGWGKITRLQYLYSA      58

DAQQTEAHLE IREDGTVGGAAQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGYG      112
                  * ** ** * ** * * * * * ** **
GPYVSNCF LRIRSDGSDVCEEDQNERNLLEFRAVALKTI AIKDVSSVRYLCMSADGKIYG      118

SLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPAPRFLPLPGLPP      172
                  * * ***   *** * * * * * * * * * *
LIRYSEEDCTFREEMDCLGYNQYRSMKHHLHIIFIQAK-PREQLDQKPSNFI PVFHRSF      177

ALPEPPGILAPQ--PPDVGSSDPLSMVGPSQG--RSPSYAS
                  * * ** **   ***
FETGDQLRSKMFSLPLESDSMDPFRMVEDVDHLVKSPSFQK

```

(57) Abstract: This invention relates to human fibroblast growth factor (hFGF-21), and to variants thereof and to polynucleotides encoding FGF-21. The invention also relates to diagnostic and therapeutic agents related to the polynucleotides and proteins, including probes and antibodies, and to methods of treating liver disease such as cirrhosis and cancer, methods of treating conditions related to thymic function, and methods of treating conditions of the testis. The invention also relates to mouse fibroblast growth factor (mFGF-21), and to variants thereof and polynucleotides encoding mFGF-21.

WO 01/36640 A3



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

In ternational Application No
PCT/US 00/31745

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/50 C12N5/10 C07K16/22 A61K38/18

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 7 C12N C07K A61K

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, WPI Data, PAJ, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL SEQUENCE LIBRARY 'Online! 16 June 1999 (1999-06-16) CARNINCI, P., ET AL. : XP002165897 accession no. AV050323 ---	41-44, 46,52, 54-56
X	DATABASE EMBL SEQUENCE LIBRARY 'Online! 27 August 1997 (1997-08-27) KODA, Y., ET AL. : "changing transcription start sites in H-type alpha (1,2) fucosyltransferase gene (FUT1) during differentiation of the human erythroid lineage" XP002165898 accession no. AB006136 --- -/--	1-4,6, 12,14-18

Further documents are listed in the continuation of box C.

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

24 April 2001

Date of mailing of the international search report

10/05/2001

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

Holtorf, S

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/31745

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 27100 A (GENENTECH INC ;BOTSTEIN DAVID (US); GODDARD AUDREY (US); GURNEY AU) 3 June 1999 (1999-06-03) the whole document	
P,X	NISHIMURA T ET AL: "IDENTIFICATION OF A NOVEL FGF, FGF-21, PREFERENTIALLY EXPRESSED IN THE LIVER" BIOCHIMICA ET BIOPHYSICA ACTA,AMSTERDAM,NL, vol. 1492, no. 1, 21 June 2000 (2000-06-21), pages 203-206, XP000979068 ISSN: 0006-3002 the whole document	1-6,12, 14-18, 41-44, 46,52, 54-56
P,X, L	WO 00 54813 A (DWARKE VARAVANI J ;RENDAHL KATHERINE (US); CHIRON CORP (US); MCGEE) 21 September 2000 (2000-09-21) the whole document	41-44, 46-52, 54-59
E	WO 01 18210 A (GENENTECH INC) 15 March 2001 (2001-03-15) the whole document	1-4, 6-12, 14-18
E	WO 01 18209 A (BURGESS CATHERINE ;QUINN KERRY E (US); RASTELLI LUCA (US); VERNET) 15 March 2001 (2001-03-15) the whole document	2-4, 15-17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/31745

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9927100 A	03-06-1999	US 6000943 A	14-12-1999
		AU 1703399 A	15-06-1999
		AU 9312198 A	05-04-1999
		EP 1032668 A	06-09-2000
		WO 9914327 A	25-03-1999
		WO 9914328 A	25-03-1999
WO 0054813 A	21-09-2000	AU 3755900 A	04-10-2000
WO 0118210 A	15-03-2001	AU 1748200 A	19-06-2000
		AU 1749800 A	04-10-2000
		AU 2399300 A	28-09-2000
		AU 2600800 A	28-09-2000
		AU 3514400 A	28-09-2000
		AU 5816799 A	03-04-2000
		WO 0053753 A	14-09-2000
		WO 0104311 A	18-01-2001
		WO 0053758 A	14-09-2000
		WO 0077037 A	21-12-2000
		WO 0073348 A	07-12-2000
		WO 0032221 A	08-06-2000
		WO 0055319 A	21-09-2000
		WO 0105836 A	25-01-2001
		WO 0053751 A	14-09-2000
		AU 1749900 A	12-07-2000
		AU 2192800 A	12-07-2000
		AU 3381600 A	28-09-2000
		AU 5922999 A	03-04-2000
		WO 0053757 A	14-09-2000
		WO 0073454 A	07-12-2000
		WO 0073452 A	07-12-2000
		WO 0109327 A	08-02-2001
WO 0116318 A	08-03-2001		
WO 0119987 A	22-03-2001		
WO 0037638 A	29-06-2000		
WO 0037640 A	29-06-2000		
WO 0075316 A	14-12-2000		
WO 0118209 A	15-03-2001	NONE	