



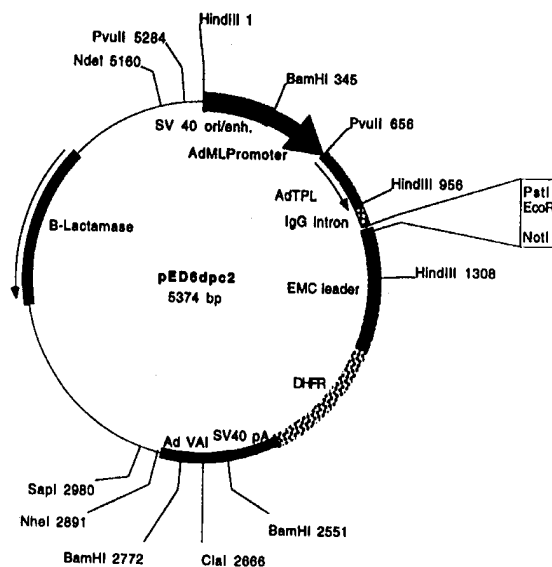
## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>6</sup> : C12N 15/12, 5/10, C07K 14/47, C12Q 1/68, A61K 38/17</p>	<p><b>A3</b></p>	<p>(11) International Publication Number: <b>WO 98/20130</b></p> <p>(43) International Publication Date: 14 May 1998 (14.05.98)</p>
<p>(21) International Application Number: PCT/US97/19857</p> <p>(22) International Filing Date: 31 October 1997 (31.10.97)</p> <p>(30) Priority Data: 08/742,973 1 November 1996 (01.11.96) US Not furnished 29 October 1997 (29.10.97) US</p> <p>(71) Applicant: GENETICS INSTITUTE, INC. [US/US]; 87 CambridgePark Drive, Cambridge, MA 02140 (US).</p> <p>(72) Inventors: JACOBS, Kenneth; 151 Beaumont Avenue, Newton, MA 02160 (US). MCCOY, John, M.; 56 Howard Street, Reading, MA 01867 (US). LAVALLIE, Edward, R.; 90 Green Meadow Drive, Tewksbury, MA 01876 (US). RACIE, Lisa, A.; 124 School Street, Acton, MA 01720 (US). MERBERG, David; 2 Orchard Drive, Acton, MA 01720 (US). TREACY, Maurice; 93 Walcott Road, Chestnut Hill, MA 02167 (US). SPAULDING, Vikki; 11 Meadowbank Road, Billerica, MA 01821 (US). AGOSTINO, Michael, J.; 26 Wolcott Avenue, Andover, MA 01810 (US).</p> <p>(74) Agent: SPRUNGER, Suzanne, A.; Genetics Institute, Inc., 87 CambridgePark Drive, Cambridge, MA 02140 (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, GE, GH, HU, IL, 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, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> <i>With international search report.</i></p> <p>(88) Date of publication of the international search report: 30 July 1998 (30.07.98)</p>	

(54) Title: SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM

## (57) Abstract

Novel proteins are disclosed.



Plasmid name: pED8dpc2  
Plasmid size: 5374 bp

Comments/References: pED8dpc2 is derived from pED8dpc1 by insertion of a new polylinker to facilitate cDNA cloning. SST cDNAs are cloned between EcoRI and NotI. pED vectors are described in Kaufman et al.(1991), NAR 19: 4485-4490.

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**INTERNATIONAL SEARCH REPORT**

International Application No

PCT/US 97/19857

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 6 C12N15/12 C12N5/10 C07K14/47 C12Q1/68 A61K38/17

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 C07K C12Q 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)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	T. FUJIWARA ET AL.: "Human fetal brain cDNA 5'end GEN-430B12" EMBL SEQUENCE DATABASE, 31 August 1995, HEIDELBERG, FRG, XP002054811 Accession no. D56480	1-8
A	L. HILLIER ET AL.: "yz37e06.s1 Homo sapiens cDNA clone 285250 3'" EMBL SEQUENCE DATABASE, 15 March 1996, HEIDELBERG, FRG, XP002054812 Accession no. N66290 --- -/--	1-8

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

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- \*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

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- \*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
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Date of the actual completion of the international search

6 February 1998

Date of mailing of the international search report

27-05-1998

Name and mailing address of the ISA

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HORNIG H.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/19857

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
A	L. HILLIER ET AL.: "zd40d05.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343113 5'" EMBL SEQUENCE DATABASE, 16 June 1996, HEIDELBERG, FRG, XP002054813 Accession no. W67393	1-8	
A	---		
A	L. HILLIER ET AL.: "zd40d05.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343113 3'" EMBL SEQUENCE DATABASE, 16 June 1996, HEIDELBERG, FRG, XP002054814 Accession no. W67150	1-8	
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A	ADAMS M D ET AL: "3,400 NEW EXPRESSED SEQUENCE TAGS IDENTIFY DIVERSITY OF TRANSCRIPTS IN HUMAN BRAIN" NATURE GENETICS, vol. 4, no. 3, pages 256-267, XP000611495 see the whole document	1-8	
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A	JACOBS K ET AL: "A novel method for isolating eukaryotic cDNA clones encoding secreted proteins." KEYSTONE SYMPOSIUM ON DENDRITIC CELLS: ANTIGEN PRESENTING CELLS OF T AND B LYMPHOCYTES, TAOS, NEW MEXICO, USA, MARCH 10-16, 1995. JOURNAL OF CELLULAR BIOCHEMISTRY SUPPLEMENT 0 (21A). 1995. 19. ISSN: 0733-1959, XP002027246 abstract no. C1-207 see abstract	1-8	
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A	EP 0 510 691 A (OSAKA BIOSCIENCE INST) 28 October 1992 see the whole document	1-8	
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A	WO 94 07916 A (MERCK & CO INC ;SCHMIDT AZRIEL (US); RODAN GIDEON A (US); RUTLEDGE) 14 April 1994 see the whole document	1-8	
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A	WO 90 05780 A (OREGON STATE) 31 May 1990 see the whole document	1-8	
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A	WO 90 14432 A (GENETICS INST) 29 November 1990 see the whole document	1-8	
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2	A	WO 96 17925 A (IMMUNEX CORP) 13 June 1996 see the whole document	1-8
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INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 97/19857

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	R.J. KAUFMAN ET AL.: "Effect of von Willebrand factor coexpression on the synthesis and secretion of factor VIII in chinese hamster ovary cells" MOL. CELL. BIOL., vol. 9, no. 3, March 1989, ASM WASHINGTON, DC,US, pages 1233-1242, XP002041592 see the whole document ---	1-8
A	R.J. KAUFMAN ET AL.: "The phosphorylation state of eucaryotic initiation factor 2 alters translation efficiency of specific mRNAs" MOL. CELL. BIOL., vol. 9, no. 3, March 1989, ASM WASHINGTON, DC,US, pages 946-958, XP002041593 see the whole document ---	1-8
A	R.J. KAUFMAN ET AL.: "Improved vectors for stable expression of foreign genes in mammalian cells by use of the untranslated leader sequence from EMC virus" NUCLEIC ACIDS RESEARCH, vol. 19, no. 16, 1991, IRL PRESS LIMITED,OXFORD,ENGLAND, pages 4485-4490, XP002041594 cited in the application see the whole document ---	1-8
A	US 5 536 637 A (JACOBS KENNETH) 16 July 1996 cited in the application see the whole document ---	1-8
P,A	WO 97 07198 A (GENETICS INSTITUT) 27 February 1997 see the whole document ---	1-8
P,A	WO 97 25427 A (GENETICS INST) 17 July 1997 see the whole document -----	1-8

## INTERNATIONAL SEARCH REPORT

...formation on patent family members

International Application No

PCT/US 97/19857

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0510691 A	28-10-92	CA 2067031 A JP 5184368 A	27-10-92 27-07-93
WO 9407916 A	14-04-94	AU 5165193 A	26-04-94
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WO 9617925 A	13-06-96	AU 4639396 A CA 2206488 A FI 972390 A NO 972455 A	26-06-96 13-06-96 05-06-97 06-08-97
US 5536637 A	16-07-96	US 5712116 A	27-01-98
WO 9707198 A	27-02-97	US 5707829 A AU 6712396 A AU 6768596 A EP 0839196 A WO 9704097 A	13-01-98 18-02-97 12-03-97 06-05-98 06-02-97
WO 9725427 A	17-07-97	AU 1532697 A	01-08-97

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 97/ 19857

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**See Annex**
  
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

**See annex**

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-8

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## 1. Claims: 1-8

A composition comprising an isolated protein encoded by a polynucleotide sequence of SEQ ID no.25; said composition further comprising a pharmaceutical acceptable carrier; a method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of said composition; a composition comprising a protein, wherein said protein comprises an amino acid sequence of SEQ ID no.26; said composition comprising a pharmaceutical acceptable carrier; a method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of said composition;

## 2. Claims: 9-10

A composition comprising an isolated protein encoded by a polynucleotide sequence selected from the group of SEQ ID no.4; a composition comprises a protein, wherein said protein comprises an amino acid sequence selected from the group of SEQ ID no.5;

## 3. Claims: 11-12

Idem as subject 2 but limited to SEQ ID nos. 7 and 8.

## 4. Claims: 13-14

Idem as subject 2 but limited to SEQ ID nos. 10 and 11.

## 5. Claims: 15-16

Idem as subject 2 but limited to SEQ ID nos. 13 and 14.

## 6. Claims: 17-18

Idem as subject 2 but limited to SEQ ID nos. 16 and 17.

## 7. Claims: 19-20

Idem as subject 2 but limited to SEQ ID nos. 19 and 20.



INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 97/19857

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. Claims: 21-22

Idem as subject 2 but limited to SEQ ID nos. 22 and 23.

Remark : Although claims 3,8 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.