



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/19093		Rae Court, Orinda, CA 94563 (US). SCHWALL, Ralph [US/US]; 400 Griffin Avenue, Pacifica, CA 94044 (US). (74) Agents: BUTING, Walter, E. et al.; Genentech, Inc., 1 DNA Way, San Francisco, CA 94080-4990 (US). (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, GM, HR, HU, ID, 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, US, 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).
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(54) Title: TIE LIGAND HOMOLOGUES

Met Arg Pro Leu Cys Val Thr Cys Trp Trp Leu Gly Leu Leu Ala
1 5 10 15

Ala Met Gly Ala Val Ala Gly Gln Glu Asp Gly Phe Glu Gly Thr
20 25 30

Glu Glu Gly Ser Pro Arg Glu Phe Ile Tyr Leu Asn Arg Tyr Lys
35 40 45

Arg Ala Gly Glu Ser Gln Asp Lys Cys Thr Tyr Thr Phe Ile Val
50 55 60

Pro Gln Gln Arg Val Thr Gly Ala Ile Cys Val Asn Ser Lys Glu
65 70 75

Pro Glu Val Leu Leu Glu Asn Arg Val His Lys Gln Glu Leu Glu
80 85 90

Leu Leu Asn Asn Glu Leu Leu Lys Gln Lys Arg Gln Ile Glu Thr
95 100 105

Leu Gln Gln Leu Val Glu Val Asp Gly Gly Ile Val Ser Glu Val
110 115 120

Lys Leu Leu Arg Lys Glu Ser Arg Asn Met Asn Ser Arg Val Thr
125 130 135

Gln Leu Tyr Met Gln Leu Leu His Glu Ile Ile Arg Lys Arg Asp
140 145 150

Asn Ala Leu Glu Leu Ser Gln Leu Glu Asn Arg Ile Leu Asn Gln
155 160 165

Thr Ala Asp Met Leu Gln Leu Ala Ser Lys Tyr Lys Asp Leu Glu
170 175 180

His Lys Tyr Gln His Leu Ala Thr Leu Ala His Asn Gln Ser Glu
185 190 195

Ile Ile Ala Gln Leu Glu Glu His Cys Gln Arg Val Pro Ser Ala
200 205 210

Arg Pro Val Pro Gln Pro Pro Pro Ala Ala Pro Pro Arg Val Tyr
215 220 225

Gln Pro Pro Thr Tyr Asn Arg Ile Ile Asn Gln Ile Ser Thr Asn
230 235 240

Glu Ile Gln Ser Asp Gln Asn Leu Lys Val Leu Pro Pro Leu
245 250 255

A

Pro Thr Met Pro Thr Leu Thr Ser Leu Pro Ser Ser Thr Asp Lys
260 265 270

Pro Ser Gly Pro Trp Arg Asp Cys Leu Gln Ala Leu Glu Asp Gly
275 280 285

His Asp Thr Ser Ser Ile Tyr Leu Val Lys Pro Glu Asn Thr Asn
290 295 300

Arg Leu Met Gln Val Trp Cys Asp Gln Arg His Asp Pro Gly Gly
305 310 315

Trp Thr Val Ile Gln Arg Arg Leu Asp Gly Ser Val Asn Phe
320 325 330

Arg Asn Trp Glu Thr Tyr Lys Gln Gly Phe Gly Asn Ile Asp Gly
335 340 345

Glu Tyr Trp Leu Gly Leu Glu Asn Ile Tyr Trp Leu Thr Asn Gln
350 355 360

Gly Asn Tyr Lys Leu Leu Val Thr Met Glu Asp Trp Ser Gly Arg
365 370 375

Lys Val Phe Ala Glu Tyr Ala Ser Phe Arg Leu Glu Pro Glu Ser
380 385 390

Glu Tyr Tyr Lys Leu Arg Leu Gly Arg Tyr His Gly Asn Ala Gly
395 400 405

Asp Ser Phe Thr Trp His Asn Gly Lys Gln Phe Thr Thr Leu Asp
410 415 420

Arg Asp His Asp Val Tyr Thr Gly Asn Cys Ala His Tyr Gln Lys
425 430 435

Gly Gly Trp Trp Tyr Asn Ala Cys Ala His Ser Asn Leu Asn Gly
440 445 450

Val Trp Tyr Arg Gly Gly His Tyr Arg Ser Arg Tyr Gln Asp Gly
455 460 465

Val Tyr Trp Ala Glu Phe Arg Gly Gly Ser Tyr Ser Leu Lys Lys
470 475 480

Val Val Met Met Ile Arg Pro Asn Pro Asn Thr Phe His
485 490 495

B

(57) Abstract

The present invention concerns isolated nucleic acid molecules encoding the TIE ligands NL1, NL5, NL8 and NL4, the proteins encoded by such nucleic acid molecules, as well as methods and means for making and using such nucleic acid and protein molecules.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/19093

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/515 C12N15/86 C12N5/10 C07K16/18
A61K38/18 A61K39/395 A61K39/44 C07K19/00 G01N33/68
G01N33/53 C12Q1/68

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 A61K G01N C12Q

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	WO 96 11269 A (REGENERON PHARMACEUTICALS, INC.) 18 April 1996 cited in the application see page 1, line 16 - page 2, line 11 see page 7, line 3 - page 9, line 3 see page 11, line 8 - page 32, line 2; examples -----	1-47



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

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"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

23 March 1999

Date of mailing of the international search report

29/03/1999

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INTERNATIONAL SEARCH REPORT

international application No.

PCT/US 98/ 19093

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:
Remark: Although claims 34, 35, 37, 38 and 43-45, as far as concerning an vivo method, and claims 32, 33, 36, and 39 are directed to a method of the human/animal body, the search has been carried out and based on the alleged of the compound/composition.
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:

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.:

Remark on Protest

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/19093

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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