

(19) World Intellectual Property Organization  
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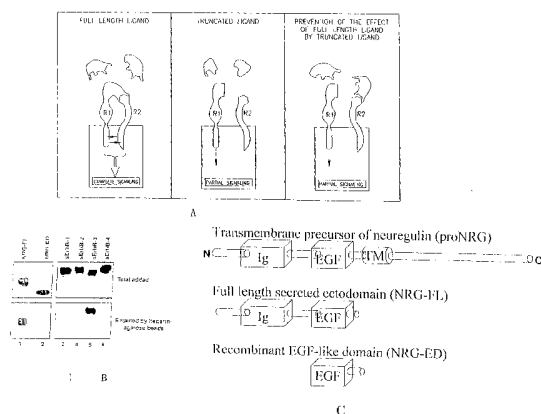
(43) International Publication Date  
20 June 2002 (20.06.2002)

PCT

(10) International Publication Number  
WO 02/048191 A3

- (51) International Patent Classification<sup>7</sup>: C07K 14/475, A61K 38/18, A61P 35/00
- (21) International Application Number: PCT/IL01/01143
- (22) International Filing Date: 11 December 2001 (11.12.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/254,153 11 December 2000 (11.12.2000) US
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- (81) Designated States (national): AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, 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, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, 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, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report: 11 December 2003
- 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.

(54) Title: INHIBITORY AGENTS DERIVED FROM SPECIFIC GROWTH FACTORS



(57) Abstract: Inhibitory agents for blocking proliferative, apoptic, mitogenic and morphogenetic processes which are derived from specific growth factors, and in particular to such agents which are derived from NDF (neuregulin). The inhibitory agents of the present invention are optionally and preferably peptides, or homologues, analogues or other related biologically active agents thereof, which are derived from at least a portion of neuregulin. More preferably, such an agent is derived from a particular fragment of neuregulin, known as the ED fragment, which includes the EGF-like domain of neuregulin. Alternatively, the agent is derived from any portion of neuregulin having the ability to bind to at least one of the ErbB-3 and ErbB-2 receptors, but lacking the ability to induce morphogenetic events. Alternatively or additionally, the agent is derived from two or more separate portions of neuregulin having these characteristics. Thus, the inhibitory agent of the present invention only causes a partial phenotypic response, but blocks the ability of full-length neuregulin to induce those aspects of the full response which are related to morphogenetic events, such as cell motility and morphogenetic behaviors



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## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/IL 01/01143

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/475 A61K38/18 A61P35/00

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 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, SEQUENCE SEARCH, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 136 558 A (FAIRBROTHER WAYNE J ET AL) 24 October 2000 (2000-10-24) Fig. 1, SEQ. No.: 1 ---	1-23
X	CHAUSOVSKY A. ET AL: "Morphogenetic activity of neuregulin requires interactions of neuregulin and its receptor ErbB-3 with heparan sulfate proteoglycans" MOL. BIOL. CELL, vol. 11, no. supplement, 9 December 2000 (2000-12-09), page 145a XP009003063 abstract --- -/--	1-23



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.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

13 January 2003

Date of mailing of the International search report

31/01/2003

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Inter I Application No

PCT/IL 01/01143

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CHAUSOVSKY ALEXANDER ET AL:                      "Morphogenetic effects of neuregulin (Neu differentiation factor) in cultured epithelial cells."                      MOLECULAR BIOLOGY OF THE CELL,                      vol. 9, no. 11, November 1998 (1998-11),                      pages 3195-3209, XP002226535                      ISSN: 1059-1524                      cited in the application                      abstract</p> <p style="text-align: center;">-----</p>	<p>1-3,5-7,                      9-13,                      15-23</p>

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/IL 01/01143

**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:  

Although claims 7-10 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.
  
2.  Claims Nos.: 11, 12, 15-20  
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:  

see FURTHER INFORMATION sheet PCT/ISA/210
  
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.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11, 12, 15-20

Present claims 11, 12, 15-20 relate to a agent defined by reference to a desirable characteristic or property, namely that it binds to one but not to all of a plurality of receptors and that it blocks a growth-factor mediated process.

The claims cover all agents having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such agents. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the agent by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely when the agent is the ED-fragment of neuregulin.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Intern	Application No
PCT/IL	01/01143

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6136558	A	24-10-2000	NONE