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31 July 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: INHIBITION OF TUMOR GROWTH BY A NEMATODE ANTICOAGULANT PROTEIN

(57) Abstract: The present invention relates to compositions and uses of nematode anticoagulant proteins (NAPs). More specifically, the invention relates to the use of rNAPc2 and rNAP5 for the inhibition of endothelial cell proliferation and the inhibition of angiogenesis. The invention also relates to methods for the treatment of angiogenesis-mediated diseases, such as cancer.



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INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/US 01/22231

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/57 C12N5/06 C12N5/08 A61P35/00 A61P7/02

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 A61L A61K C12N

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, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 872 098 A (LAROCHE YVES RENE ET AL) 16 February 1999 (1999-02-16) column 2, line 58 - line 62 column 14, line 51 - line 57 column 16, line 16 - line 23 column 37, line 36 - line 65 column 38, line 13; examples 3,15 ---	1-16
Y	US 5 981 471 A (GREEN SHAWN J ET AL) 9 November 1999 (1999-11-09) claims --- -/--	1-34

☒ 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

26 February 2003

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20/03/2003

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Int nal Application No
PCT/US 01/22231

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	STANSSENS PATRICK ET AL: "Anticoagulant repertoire of the hookworm Ancylostoma caninum." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 93, no. 5, 1996, pages 2149-2154, XP002229520 1996 ISSN: 0027-8424 page 2149, column 1, line 19-21 -----	1-34

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/22231**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 1-3 (as far as in vivo application is concerned), 5-34 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.: 1-7,9,11-34 (all partially)
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.: 1-7,9,11-34 (all partially)

Present claims 1-7,9,11-34 are related to the prevention or treatment of diseases which are not clearly defined, namely conditions related to "inhibition of endothelial cell proliferation", "an endothelial cell proliferative mediated disease", "inhibition of angiogenesis", or "angiogenesis mediated disease", and "cancer". Due to the functional definition of the claimed subject-matter, the scope of protection of the claims 1-7,9,11-34 is obscure and not limited to the treatment of said specified conditions in the description and/or the claims but, by contrast, embraces an undefined number of other conditions allegedly capable of being improved or prevented by the administration of nematode anticoagulant protein. Therefore, the claims 1-7,9,11-34 lack support (Article 6 PCT) and the application lacks disclosure (Article 5 PCT). 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 above expressions are vague and unclear and leave the reader in doubt as to the meaning of the technical feature to which they refer, thereby rendering the definition of the subject-matter of claims 1-7,9,11-34 unclear (Article 6 PCT). 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 the use of nematode anticoagulant protein (with focus on NAPc2 and NAP5) in the therapy of diseases as in claims 8,10; and with due regard to the general concept of the invention.

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

Information on patent family members

International Application No

PCT/US 01/22231

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