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(54) Title: NUCLEAR PORE PROTEIN NUP88 AS A NOVEL TARGET

(57) Abstract: The present invention relates to the use of nucleoporin 88 as a novel target within the signaling pathway of NF- $\kappa$ B. It provides a new therapeutic approach for a broad range of diseases in which NF- $\kappa$ B is involved. This is for instance the case for inflammatory diseases, such as rheumatoid arthritis, asthma, inflammatory bowel disease, systemic inflammatory response syndrome etc. and cancer. Pharmaceutical compositions which comprise a compound which interferes with nucleoporin 88 activity or expression are also part of the invention.

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# INTERNATIONAL SEARCH REPORT

International Application No  
/NL 03/00783

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 G01N33/564 G01N33/574				
According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 G01N				
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, EMBASE				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	ZHANG H ET AL: "EXPRESSION OF P16, P27, P53, P73 AND NUP88 PROTEINS IN MATCHED PRIMARY AND METASTATIC MELANOMA CELLS" INTERNATIONAL JOURNAL OF ONCOLOGY, EDITORIAL ACADEMY OF THE INTERNATIONAL JOURNAL OF ONCOLOGY,, GR, vol. 21, no. 1, July 2002 (2002-07), pages 43-48, XP009006694 ISSN: 1019-6439 abstract; figure 4; table 1  <div style="text-align: center;">----- -/--</div>	9		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <span style="margin-left: 200px;"><input type="checkbox"/> Patent family members are listed in annex.</span>				
° Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> <li>*A* document defining the general state of the art which is not considered to be of particular relevance</li> <li>*E* earlier document but published on or after the international filing date</li> <li>*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)</li> <li>*O* document referring to an oral disclosure, use, exhibition or other means</li> <li>*P* document published prior to the international filing date but later than the priority date claimed</li> </ul> </td> <td style="width: 50%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> <li>*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</li> <li>*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</li> <li>*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.</li> <li>*&amp;* document member of the same patent family</li> </ul> </td> </tr> </table>			<ul style="list-style-type: none"> <li>*A* document defining the general state of the art which is not considered to be of particular relevance</li> <li>*E* earlier document but published on or after the international filing date</li> <li>*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)</li> <li>*O* document referring to an oral disclosure, use, exhibition or other means</li> <li>*P* document published prior to the international filing date but later than the priority date claimed</li> </ul>	<ul style="list-style-type: none"> <li>*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</li> <li>*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</li> <li>*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.</li> <li>*&amp;* document member of the same patent family</li> </ul>
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Date of the actual completion of the international search  <div style="text-align: center; font-size: 1.2em;">19 October 2004</div>		Date of mailing of the international search report  <div style="text-align: center; font-size: 1.2em;">02/11/2004</div>		
Name and mailing address of the ISA European Patent Office, P.B. 5618 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  <div style="text-align: center; font-size: 1.2em;">Vanmontfort, D</div>		

INTERNATIONAL SEARCH REPORT

International Application No

.../NL 03/00783

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MARTINEZ N ET AL: "The nuclear pore complex protein Nup88 is overexpressed in tumor cells"                      CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 59, no. 21, 1 November 1999 (1999-11-01), pages 5408-5411, XP002233676                      ISSN: 0008-5472                      cited in the application                      the whole document</p>	1-12
A	<p>GOULD V E ET AL: "A novel, nuclear pore-associated, widely distributed molecule overexpressed in oncogenesis and development"                      AMERICAN JOURNAL OF PATHOLOGY, PHILADELPHIA, PA, US, vol. 157, no. 5, November 2000 (2000-11), pages 1605-1613, XP002233677                      ISSN: 0002-9440                      cited in the application                      abstract; figures 1,2; table 1</p>	1-12
A	<p>GOULD V E ET AL: "NUP88 (KARYOPORIN) IN HUMAN MALIGNANT NEOPLASMS AND DYSPLASIAS: CORRELATIONS OF IMMUNOSTAINING OF TISSUE SECTIONS, CYTOLOGIC SMEARS, AND IMMUNOBLOT ANALYSIS"                      COMPUTATIONAL LINGUISTICS, CAMBRIDGE, MA, US, vol. 33, no. 5, May 2002 (2002-05), pages 536-544, XP009006689                      the whole document</p>	1-12
A	<p>FORNEROD M: "The human homologue of yeast CRM1 is in a dynamic subcomplex with CAN/Nup214 and a novel nuclear pore component Nup88"                      EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 16, no. 4, 17 February 1997 (1997-02-17), pages 807-816, XP002123306                      ISSN: 0261-4189                      cited in the application                      the whole document</p>	1-12

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/NL 03/00783

## 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.: 1-6 for IA  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 1-6 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compound.
2.  Claims Nos.: 1-3,7  
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.1

Although claims 1-6 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compound.

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## Continuation of Box I.2

Claims Nos.: 1-3,7

Present claims 1-3 and 7 relate to a compound defined by reference to a desirable characteristic or property, namely a compound which interferes with Nup88 activity or expression.

The claims cover all compounds 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 compounds. 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 compound 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 those parts relating to the compounds as mentioned in the description at pages 7-8, i.e. antibodies against Nup88 and an antisense oligonucleotide or nucleic acid which is complementary to at least a functional part of a Nup88 RNA.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.