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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C12N 9/88, C07K 16/40 | A3

(11) International Publication Number: **WO 00/24913**

(43) International Publication Date: 4 May 2000 (04.05.00)

(21) International Application Number: PCT/US99/24879

(22) International Filing Date: 22 October 1999 (22.10.99)

(30) Priority Data:

09/177,776	23 October 1998 (23.10.98)	US
09/178,115	23 October 1998 (23.10.98)	US

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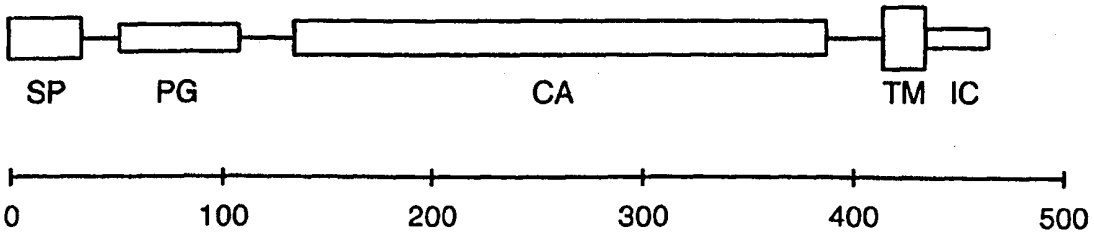
(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, 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).

Published
With international search report.

(88) Date of publication of the international search report:
14 September 2000 (14.09.00)

(54) Title: MN GENE AND PROTEIN



(57) Abstract

Identified herein is the location of the MN protein binding site, and MN proteins/polypeptides that compete for attachment to vertebrate cells with immobilized MN protein. Such MN proteins/polypeptides prevent cell–cell adhesion and the formation of intercellular contacts. The MN protein binding site is a therapeutic target that can be blocked by organic or inorganic molecules, preferably organic molecules, more preferably proteins/polypeptides that specifically bind to that site. Therapeutic methods for inhibiting the growth of preneoplastic/neoplastic vertebrate cells that abnormally express MN protein are disclosed. Vectors are provided that encode the variable domains of MN–specific antibodies and a flexible linker polypeptide separating those domains. Further vectors are disclosed that encode a cytotoxic protein/polypeptide operatively linked to the MN gene promoter, and which vectors preferably further encode a cytokine. The MN gene promoter is characterized, and the binding site for a repressor of MN transcription is disclosed.

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INTERNATIONAL SEARCH REPORT

Interr. nal Application No
PCT/US 99/24879

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N9/88 C07K16/40

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 C12N C07K

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.
X	ZAVADA, J. ET AL.: "Transient transformation of mammalian cells by MN protein, a tumor-associated cell adhesion molecule with carbonic anhydrase activity" INTERNATIONAL JOURNAL OF ONCOLOGY, vol. 10, no. 4, April 1997 (1997-04), pages 857-863, XP000909801 the whole document ---	1-4, 10-19
X	WO 95 34650 A (CIBA CORNING DIAGNOSTICS CORP ;INST OF VIROLOGY (SK); ZAVADA JAN () 21 December 1995 (1995-12-21) cited in the application page 3, line 4 -page 5, line 37; figure 1 page 56, line 6 -page 61, line 16 page 29, line 17 -page 30, line 30 page 44, line 30 -page 46, line 2	12-29
A	examples 1,4 --- -/--	1-11

[X] Further documents are listed in the continuation of box C.

[X] 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)

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 June 2000	23.06.00

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Kaas, V

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Interr. nal Application No
PCT/US 99/24879

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	OPAVSKY, R.: "Human MN/CA9 gene, a novel member of carbonic anhydrase family: structure and exon to protein domain relationships" GENOMICS, vol. 33, no. 3, 1 May 1996 (1996-05-01), pages 480-487, XP000909773	12-19, 24-27
A	the whole document	1-11
X	PASTOREK ET AL: "Cloning and characterization of MN, a human tumor-associated protein with a domain homologous to carbonic anhydrase and a putative helix-loop-helix DNA binding segment" ONCOGENE,GB,BASINGSTOKE, HANTS, vol. 9, no. 10, October 1994 (1994-10), pages 2877-2888, XP002131890 ISSN: 0950-9232	12-19
A	the whole document	1-11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/24879

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:

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:

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:

see additional sheet

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.

Continuation of Box I.2

Present claims 1 and 28 relate to a compound/complex defined by reference to a desirable characteristic or property, namely the ability to specifically bind to a site on the MN protein and the ability to inhibit the adhesion of cells to MN protein (claim 1) and the ability to bind and repress the MN gene promoter.

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 product/compound/method/apparatus 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, as regards claim 1, 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 heptapeptides prepared in example 3 on pages 70-71. Given that the application fails to identify any "repressor complex", the search concerning claim 28 has been restricted to antisense constructs as defined on pages 38-39 of the description.

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-11

   An organic or inorganic molecule that binds specifically to a site on a MN protein and inhibits the adhesion of cells to the MN protein in vitro.

2. Claims: 12-19

   A MN protein or MN polypeptide which prevents the formation of intracellular contacts and the adhesion of vertebrate cells to each other.

3. Claims: 20-23

   A vector comprising a nucleic acid encoding the variable domains of a MN-specific antibody wherein said domains are separated by a flexible linker polypeptide.

4. Claims: 24-27

   A vector comprising a nucleic acid that encodes a cytotoxic protein operably linked to a MN gene promoter.

5. Claims: 28-30

   A repressor complex that binds to the MN gene promoter.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr. nal Application No
PCT/US 99/24879

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9534650 A	21-12-1995	US 5981711 A	09-11-1999
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		AU 2861695 A	05-01-1996
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		US 6027887 A	22-02-2000