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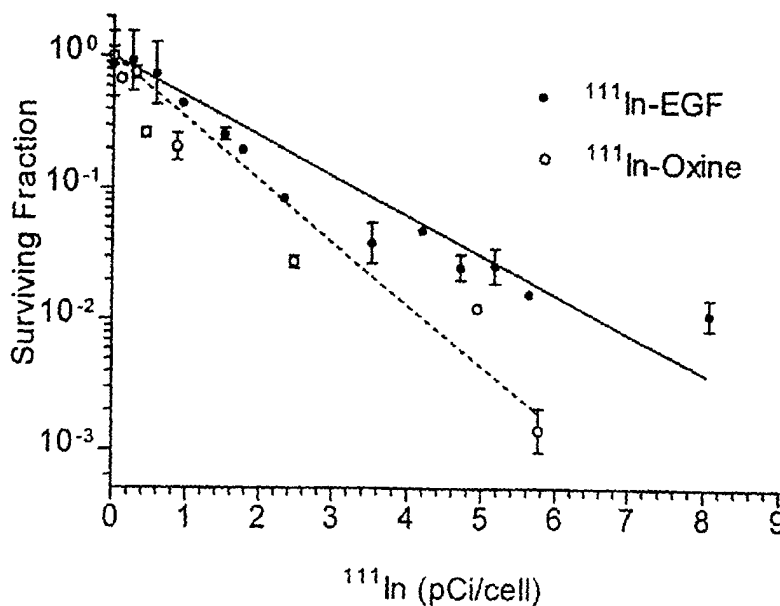
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A RADIOLABELLED LIGAND FOR SELECTIVE INTRODUCTION INTO THE NUCLEUS OF A CANCER CELL



(57) Abstract: The invention is a radiolabelled ligand for introducing an Auger electron emitting radionuclide into the nucleus of a cancer cell. The ligand binds selectively to a cell surface receptor that is unique to a cancer cell or which is overexpressed on a cancer cell. An Auger electron emitting radionuclide is bonded to the ligand either directly or by means of a chelator. The radiolabelled ligand is internalized by the cell upon binding to the receptor, and a sufficient portion of the ligands so internalized are transported to the nucleus to provide a lethal dose of radiation to it.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 97/00909

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 A61K51/08

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 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SANDRINE REMY ET AL: "A NEW RADIOLIGAND FOR THE EPIDERMAL GROWTH FACTOR RECEPTOR: 111IN LABELED HUMAN EPIDERMAL GROWTH FACTOR DERIVATIZED WITH A BIFUNCTIONAL METAL-CHELATING PEPTIDE" BIOCONJUGATE CHEMISTRY, vol. 6, no. 6, 1 November 1995, pages 683-690, XP000542534 see abstract see figures 1-3 see page 688, right-hand column	1-7
X	WO 91 01144 A (SANDOZ AG ;SANDOZ AG (DE); SANDOZ LTD (CH)) 7 February 1991 see examples 4,11,13	1-7

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>	<p>*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</p> <p>*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</p> <p>*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.</p> <p>*Z* document member of the same patent family</p>
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Date of the actual completion of the international search	Date of mailing of the international search report
17 June 1998	08 07 1998

Name and mailing address of the ISA 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	Authorized officer Dullaart, A
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INTERNATIONAL SEARCH REPORT

International Application No
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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>GOLDENBERG A ET AL: "Imaging of human tumor xenografts with an indium-111-labeled anti-epidermal growth factor receptor monoclonal antibody." J NATL CANCER INST, NOV 1 1989, VOL. 81, NO. 21, PAGE(S) 1616-25, XP002068410 see abstract see page 161, right-hand column, last paragraph - page 162, left-hand column ---</p>	1-7
X	<p>SAGA T ET AL: "SCINTIGRAPHIC DETECTION OF OVEREXPRESSED C-ERB-B-2 PROTOONCOGENE PRODUCTS BY A CLASS-SWITCHED MURINE ANTI-C-ERB-B-2 PROTEIN MONOCLONAL ANTIBODY" CANCER RES, 1991, VOL. 51, NO. 3, PAGE(S) 990-994., XP002068411 see abstract see paragraph RESULTS ---</p>	1-7
X	<p>DERUI L ET AL: "RADIOTOXICITY OF IODINE-125-LABELED MONOCLONAL ANTIBODY 425 AGAINST CANCER CELLS CONTAINING EPIDERMAL GROWTH FACTOR RECEPTOR" AM J CLIN ONCOL, 1992, VOL. 15, NO. 4, PAGE(S) 288-294., XP002068412 see page 288 see paragraph RESULTS ---</p>	1-7
X	<p>DADPARVAR S ET AL: "Indium-111-labeled anti-EGFr-425 scintigraphy in the detection of malignant gliomas." CANCER, 1-2-1994, VOL. 73, NO. 3 SUPPL, PAGE(S) 884-9, XP002068413 see abstract see paragraph RESULTS see paragraph DISCUSSION ---</p>	1-7
X	<p>DE JONG M ET AL: "HANDLING OF IODINE-125 TYR-3-OCTREOTIDE INDIUM-111 DTPA -D-PHE-1-OCTREOTIDE AND IODINE-125 EPIDERMAL GROWTH FACTOR EGF BY THE ISOLATED PERFUSED RAT LIVER" 39TH ANNUAL MEETING OF THE SOCIETY OF NUCLEAR MEDICINE, LOS ANGELES, CALIFORNIA, USA, JUNE 9-12, 1992., XP002068414 see abstract & J NUCL MED, 1992, VOL. 33, NO. 5, SUPPL., PAGE(S) 955, ABSTRACT NO. 548, see the whole document --- -/--</p>	1-7

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 97/00909

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>ENNIS B W ET AL: "THE EGF RECEPTOR SYSTEM AS A TARGET FOR ANTITUMOR THERAPY" CANCER INVESTIGATION, vol. 9, no. 5, 1991, pages 553-562, XP000619907 see the whole document</p> <p style="text-align: center;">---</p>	1-7
Y,P	<p>CAPALA J ET AL: "RADIOLABELING OF EPIDERMAL GROWTH FACTOR WITH 99MTC AND IN VIVO LOCALIZATION FOLLOWING INTRACEREBRAL INJECTION INTO NORMAL AND GLIOMA-BEARING RATS" BIOCONJUGATE CHEMISTRY, vol. 8, no. 3, May 1997, pages 289-295, XP000689386 see the whole document</p> <p style="text-align: center;">-----</p>	1-7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 97/00909

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.: **1-5 and 7 in part**
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

Claims Nos.: 1-5 and 7 in part

In view of the large number of compounds, which are defined by the general definition in the independent claims, the search had to be restricted for economic reasons. The search was limited to the compounds for which pharmacological data was given and/or the compounds mentioned in the claims, and to the general idea underlying the application. (see Guidelines, Chapter III, paragraph 2.3).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 97/00909

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9101144 A	07-02-1991	AT 120374 T	15-04-1995
		AU 638043 B	17-06-1993
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		CA 2032499 A	21-01-1991
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		DE 69018226 T	21-09-1995
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		IE 67637 B	17-04-1996
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		US 5686410 A	11-11-1997