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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,
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GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, 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, NI, NO, NZ, OM, PG, PH,
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DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT,
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ance Notes on Codes and Abbreviations" appearing at the begin-
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(54) Title: DIAGNOSTICS AND THERAPEUTICS FOR DISEASES ASSOCIATED WITH HUMAN ENDOTHELIAL DIFFER-
ENTIATION, SPHINGOLIPID G-PROTEIN-COUPLED RECEPTOR 3 (EDG3)

(57) Abstract: The invention provides a human EDG3 which is associated with the hematological diseases, cardiovascular diseases,
disorders of the peripheral and central nervous system, urology diseases, cancer diseases. The invention also provides assays for the
identification of compounds useful in the treatment or prevention of hematological diseases, cardiovascular diseases, disorders of
the peripheral and central nervous system, urology diseases, cancer diseases. The invention also features compounds which bind to
and/or activate or inhibit the activity of EDG3 as well as pharmaceutical compositions comprising such compounds.



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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/12120

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 G01N33/573 A61K38/00 A61K38/43				
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 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, Sequence Search, BIOSIS, EMBASE, WPI Data, PAJ				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	MAZURAI D. ET AL: "Cell type-specific localization of human cardiac S1P receptors" JOURNAL OF HISTOCHEMISTRY AND CYTOCHEMISTRY, vol. 50, no. 5, May 2002 (2002-05), pages 661-669, XP0009029256 the whole document ----- -/--	1-18,22, 23		
<table style="width:100%; border:none;"> <tr> <td style="width:50%; border:none;"><input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.</td> <td style="width:50%; border:none;"><input checked="" type="checkbox"/> Patent family members are listed in annex.</td> </tr> </table>			<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.			
° Special categories of cited documents :				
<table style="width:100%; border:none;"> <tr> <td style="width:50%; border:none;"> *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 </td> <td style="width:50%; border:none;"> *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. *&* document member of the same patent family </td> </tr> </table>			*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. *&* document member of the same patent family
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. *&* document member of the same patent family			
Date of the actual completion of the international search <p align="center">20 April 2004</p>		Date of mailing of the international search report <p align="center">07/05/2004</p>		
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 <p align="center">Luis Alves, D</p>		

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/12120

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZHANG G ET AL: "Comparative analysis of three murine G-protein coupled receptors activated by sphingosine-1-phosphate" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 227, no. 1, 4 February 1999 (1999-02-04), pages 89-99, XP004155772 ISSN: 0378-1119 page 93, right-hand column, paragraph 1 - page 95, left-hand column, paragraph 2; figure 4	1-18,22, 23
X	----- PYNE S ET AL: "REVIEW ARTICLE SPHINGOSINE 1-PHOSPHATE SIGNALLING IN MAMMALIAN CELLS" BIOCHEMICAL JOURNAL, THE BIOCHEMICAL SOCIETY, LONDON, GB, vol. 349, 2000, pages 385-402, XP000939036 ISSN: 0264-6021 abstract page 389, right-hand column, paragraph 4 - page 391, left-hand column, paragraph 3 page 396, right-hand column, last paragraph - page 399, left-hand column, last paragraph	1-18,22, 23
X	----- US 6 130 067 A (TSUI PING) 10 October 2000 (2000-10-10) cited in the application Seq id no 1 column 2, last paragraph - column 3, paragraph 2 column 10, paragraph 3 - column 14, paragraph 3 & DATABASE EMBL 20 May 2001 (2001-05-20), Database accession no. AR112475 abstract	1-18,22, 23
X	----- RACKE K ET AL: "Potential role of EDG receptors and lysophospholipids as their endogenous ligands in the respiratory tract" PULMONARY PHARMACOLOGY AND THERAPEUTICS, vol. 13, no. 3, 2000, pages 99-114, XP002277298 & ISSN: 1094-5539 abstract page 104, left-hand column, paragraph 1 - paragraph 3 page 107, left-hand column, paragraph 2 - paragraph 4 page 109, left-hand column, paragraph 3 - right-hand column, last paragraph	1-18,22, 23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/12120

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.: 19-21, 24-26
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.: 19-21, 24-26

Claims 19 to 21 concern compositions comprising compounds which are broadly defined in terms of their function. The functional statements do not enable the skilled person to determine the technical characteristics of the compounds. Therefore, said claims do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The description fails to give any specific examples of compounds which would fulfill the desired functions. Therefore said claims also lack support in the description as required by Article 6 PCT, as their scope is broader than justified by the description and drawings.

Thus, no meaningful search could be performed for said claims.

For the same reasons as above, the use claims 24 and 26 do not have a clearly defined scope and do not find support in the description (Article 6 PCT).

The same objections apply to claim 25 and furthermore the performance of the claimed method depends on the achievement of a result in step (i) - identification of a regulator of EDG3 - for which no specific example is present in the description.

This lack of clarity and support (Article 6 PCT) is such as to render a meaningful search for claims 24 to 26 impossible.

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/12120

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6130067	A	10-10-2000	EP 1077996 A1	28-02-2001
			JP 2002515233 T	28-05-2002
			WO 9960019 A1	25-11-1999
			US 6344542 B1	05-02-2002
