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(71) Applicant (*for all designated States except US*): **DI-ADEXUS, INC.** [US/US]; 343 Oyster Point Boulevard, South San Francisco, CA 94080 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **MACINA, Roberto, A.** [AR/US]; 4118 Crescendo Avenue, San Jose, CA 95136 (US). **PILLAI, Rajeswari** [IN/US]; 1321 Marshall Street, #517, Redwood City, CA 94063 (US).

(74) Agents: **LICATA, Jane, Massey** et al.; Licata & Tyrrell P.C., 66 E. Main Street, Marlton, NJ 08053 (US).

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(54) Title: METHOD OF DIAGNOSING, MONITORING, STAGING, IMAGING AND TREATING COLON CANCER

(57) Abstract: The invention relates to CSG polypeptides, polynucleotides encoding the polypeptides, methods for producing the polypeptides, in particular by expressing the polynucleotides, and agonists and antagonists of the polypeptides. The invention further relates to methods for utilizing such polynucleotides, polypeptides, agonists and antagonists for applications, which relate, in part, to research, diagnostic and clinical arts.



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INTERNATIONAL SEARCH REPORT

International Application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 C12N9/12 C07K16/00 A61K38/43 A61K39/395
 G01N33/573 G01N33/574

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 C12Q

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, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 20587 A (LUDWIG INST CANCER RES) 13 April 2000 (2000-04-13) SEQ ID No. 23 claim 57	1,7,8,12
X	WO 97 14966 A (MOUNT SINAI HOSPITAL CORP) 24 April 1997 (1997-04-24) SEQ ID No. 1 and 2 --- -/--	1,7,8,12

☒ 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.

& document member of the same patent family

Date of the actual completion of the international search

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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

Marinoni, J-C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/20724

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	IKEGAKI N ET AL: "MOLECULAR CHARACTERIZATION AND CHROMOSOMAL LOCALIZATION OF DRT (EPHT3): A DEVELOPMENTALLY REGULATED HUMAN PROTEIN-TYROSINE KINASE GENE OF THE EPH FAMILY" HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 4, no. 11, November 1995 (1995-11), pages 2033-2045, XP000946771 ISSN: 0964-6906 the whole document ---	1,7,8,12
X	KIYOKAWA E ET AL: "OVEREXPRESSION OF ERK AN EPH FAMILY RECEPTOR PROTEIN TYROSINE KINASE IN VARIOUS HUMAN TUMORS" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 54, 15 July 1994 (1994-07-15), pages 3645-3650, XP002070092 ISSN: 0008-5472 page 3647, right-hand column, line 16 -page 3649, right-hand column, line 6; figure 1B ---	1,7,8,12
A	WO 96 39541 A (HUMAN GENOME SCIENCES INC ;LI YI (US); SOPPET DANIEL R (US); DILLO) 12 December 1996 (1996-12-12) ---	
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A	WO 99 60161 A (DIADEXUS LLC ;SUN YONGMING (US); YANG FEI (US); MACINA ROBERTO A ()) 25 November 1999 (1999-11-25) ---	
A	WO 00 07632 A (MACINA ROBERTO A ;SUN YONGMING (CN); RECIPON HERVE (FR); DIADEXUS) 17 February 2000 (2000-02-17) ---	
A	WO 00 20640 A (DIADEXUS LLC ;MACINA ROBERTO A (US)) 13 April 2000 (2000-04-13) ---	
P,X	WO 00 53216 A (SMITHKLINE BEECHAM BIOLOG ;VINALS Y DE BASSOLS CARLOTA (BE)) 14 September 2000 (2000-09-14) claims 1-16; examples 1-6 --- -/--	1-14

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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.
P,X	OBA SUELI M ET AL: "Genomic structure and loss of heterozygosity of EPHB2 in colorectal cancer." CANCER LETTERS, vol. 164, no. 1, 10 March 2001 (2001-03-10), pages 97-104, XP002242706 ISSN: 0304-3835 the whole document ---	1-14
P,X	MORIMOTO M. ET AL: "Differential gene expression of highly metastatic variants and clones of mouse colon adenocarcinoma cells" CLINICAL & EXPERIMENTAL METASTASIS, vol. 17, no. 9, 24 September 2000 (2000-09-24), page 750 XP009011581 abstract -----	1-14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/20724

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.: 2-6, 11-13 partially
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 11 and 12 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:

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.:
1-14 all partially

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

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

Invention 1: claims 1-14 all partially

The nucleic acids of SEQ ID No. 1 and 16, the polypeptides they encode, uses and methods, antibodies and vaccines related thereto.

Inventions 2-18: claims 1-14 all partially

The nucleic acid of SEQ ID No. 2-15 and 17-19, the polypeptides they each encode, uses and methods, antibodies and vaccines related thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 2-6 are directed to a diagnostic method practised on the human/animal body, and include a step of "identifying a patient with colon cancer", i.e. a diagnostic step, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 11-13 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.

Continuation of Box I.1

Claims Nos.: 2-6, 11-13 partially

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body

Continuation of Box I.2

Claims Nos.: 11 and 12 partially

Present claim 11 relates to a method defined by reference to a desirable characteristic or property, namely that it comprises the administering to a patient a compound that downregulates expression or activity of a CSG. The claims cover all methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such methods. 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 method 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 methods wherein an antibody directed to a CSG polypeptide encoded by the nucleic acids of claim 1 or an antisense nucleotide directed to said polynucleotides of claim 1 is administered to a patient.

Additionally, claim 12 is directed to a method of inducing an immune response against a targeted cell expressing a CSG of claim 1 comprising delivering to a patient an undefined CSG polypeptide. As it appears that at least some of the CSG polynucleotides of claim 1 are expressed by many cell types, and that the term "CSG polypeptide" does not impose any limitation on the polypeptide to be administered, the claim lacks clarity

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

contrary to Article 6 PCT. Search is therefore restricted to those methods of claim 13 wherein the polypeptide to be administered is encoded by the nucleic acids of claim 1.

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

International Application No

PCT/US 01/20724

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