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*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: MUTANT FORMS OF THE TGF-B TYPE II RECEPTOR WHICH BIND ALL TGF-B ISOFORMS AND THE USE THEREOF

(57) Abstract: The present invention relates to gene expression in normal cells and cells of tumors and particularly to mutant forms of the TGF- β II receptor receptor which bind all TGF- β isoforms. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating a disease associated with a mutated TGF- β , type II receptor, e.g. a tumor.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/08562

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/71 C12N15/12 C07K16/28 C12N5/12 C12N15/63
A01K67/02 C12Q1/68 A61K38/17 A61K31/711 A61K39/395
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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 C07K C12N A01K C12Q A61K A61P

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	ROTZER DIANA ET AL: "Type III TGF-beta receptor-independent signalling of TGF-beta2 via TbetaRII-B, an alternatively spliced TGF-beta type II receptor." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 20, no. 3, 1 February 2001 (2001-02-01), pages 480-490, XP002232820 ISSN: 0261-4189 the whole document --- -/--	1-9, 20-28

☒ 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

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"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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05. 06. 2003

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/08562

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 13705 A (BIOPH BIOTECH ENTW PHARM GMBH ;KRIEGELSTEIN KERSTIN (DE)) 16 March 2000 (2000-03-16) page 5, line 4 - line 5 page 10, line 29 -page 11, line 2 claims examples ----	1-9, 20-28
A	HIRAI R ET AL: "A HUMAN TRANSFORMING GROWTH FACTOR-BETA TYPE II RECEPTOR THAT CONTAINS AN INSERTION IN THE EXTRACELLULAR DOMAIN" EXPERIMENTAL CELL RESEARCH, SAN DIEGO, CA, US, vol. 223, 1996, pages 135-141, XP000579131 ISSN: 0014-4827 cited in the application the whole document ----	1-9, 20-28
A	NIKAWA J-I: "A CDNA ENCODING THE HUMAN TRANSFORMING GROWTH FACTOR SS RECEPTOR SUPPRESSES THE GROWTH DEFECT OF A YEAST MUTANT" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 149, 1994, pages 367-372, XP000887377 ISSN: 0378-1119 cited in the application the whole document ----	1-9, 20-28
A	SUZUKI A ET AL: "CLONING OF AN ISOFORM OF MOUSE TGF-BETA TYPE II RECEPTOR GENE" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 355, 1994, pages 19-22, XP000909494 ISSN: 0014-5793 the whole document -----	1-9, 20-28

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-9,20-28

A pharmaceutical composition comprising a compound which is capable of binding the TGF-beta isoforms TGF-beta 1,2 and 3 or a nucleic acid molecule encoding a polypeptide having such an activity for preventing or treating a disorder associated with an abnormal TGF-beta expression or an abnormal interaction of TGF-beta with their receptor(s).

2. Claims: 10-13,16-18,29,30

An antibody which is capable of specifically binding to a mutant TGF-beta type II receptor but which does not bind to wild type TGF-beta receptor; a hybridoma producing the antibody; a pharmaceutical composition comprising the antibody and the uses of the antibody.

3. Claim : 14

A transgenic non human animal containing an insertion of TGF-beta1 encoding cDNA within the first exon of the TGF-beta2 encoding gene.

4. Claim : 15

A transgenic non-human animal which as a knockout animal as regards the native or a mutant TGF-beta type II receptor encoding gene.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/08562

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:
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.:
1-9, 20-28

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/08562

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0013705 A	16-03-2000	AU 5857899 A	27-03-2000
		CA 2342208 A	16-03-2000
		EP 1109579 A	27-06-2001
		AU 1040600 A	04-10-2000
		WO 0054804 A	21-09-2000
