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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: MAXS AS MODIFIERS OF THE AXIN PATHWAY AND METHODS OF USE

(57) Abstract: Human MAX genes are identified as modulators of the AXIN pathway, and thus are therapeutic targets for disorders associated with defective AXIN function. Methods for identifying modulators of AXIN, comprising screening for agents that modulate the activity of MAX are provided.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/24560

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/00, 33/53; C07K 14/00
US CL : 435/7.8, 375; 530/350; 800/3

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)
U.S. : 435/7.8, 375; 530/350; 800/3

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 practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FAGOTTO F, et al. Domains of Axin involved in protein-protein interactions, Wnt pathway inhibition, and intracellular localization. J. Cell biol. 17 May 1999, Vol. 145, No. 4, pages 741-756; see entire document.	1-5, 7, 11, 12, and 16-19
Y,P	RUI H-L, et al. SUMO-1 modification of the C-terminal KVEKVD of Axin is required for JNK activation but has no effect on Wnt signaling. J. Biol. Chem. 08 November 2002, Vol. 277, No. 45, pages 42981-42986; see entire document.	1-5, 7, 11, 12, and 16-19
Y,T	RUIZ S, et al. Functional link between retinoblastoma family of proteins and the Wnt signaling pathway in mouse epidermis. Developmental Dynamics. 2004, Vol. 230, pages 410-418; see entire document.	1-5, 7, 11, 12, and 16-19
Y,T	SHIBAMOTO S, et al. A blockade in Wnt signaling is activated following the differentiation of F9 teratocarcinoma cells. Experimental Cell Research. 2004, Vol. 292, pages 11-20; see entire document.	1-5, 7, 11, 12, and 16-19

☒ Further documents are listed in the continuation of Box C. ☐ See patent family 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 application or patent 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	Date of mailing of the international search report
27 September 2004 (27.09.2004)	13 OCT 2004
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Stephen L. Rawlings, Ph.D. Telephone No. (703) 308-0196

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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.
Y	HSU W, et al. Impaired mammary gland and lymphoid development caused by inducible expression of Axin in transgenic mice. J. Cell Biol. 10 December 2001, Vol. 155, No. 6, pages 1055-1064; see entire document.	1-5, 7, 11, 12, and 16-19
Y	NISHIDA T, et al. Characterization of a novel mammalian SUMO-1/Smt3-specific isopeptidase, a homologue of rat Axam, which is an Axin-binding protein promoting beta-catenin degradation. J. Biol. Chem. 19 October 2001, Vol. 276, No. 42, pages 39060-39066; see entire document.	1-5, 7, 11, 12, and 16-19
Y	KADOYA T, et al. Inhibition of Wnt signaling pathway by a novel Axin-binding protein. J. Biol. Chem. 24 November 2000, Vol. 275, No. 47, pages 37030-37037; see entire document.	1-5, 7, 11, 12, and 16-19

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim 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. ☐ Claim 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:
Please See Continuation 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.: Please See Continuation Sheet

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12 and 16-19, drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing an expression assay system.

Group II, claim(s) 13-15 and 20-22, drawn to a method for modulating a AXIN pathway of a cell, wherein said method comprises contacting a cell with a candidate modulator that specifically binds to a MAX polypeptide.

Group III, claim(s) 20-22, drawn to a method for modulating a AXIN pathway in a cell, wherein said method comprises contacting a cell with a candidate modulator that specifically binds to a nucleic acid molecule.

Group IV, claim(s) 23 and 24, drawn to a method for diagnosing a disease.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Group I:

Species A, claim(s) 1-5, 7, 11, 12, and 16-19, insofar as the claims are drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing a binding assay system.

Species B, claim(s) 1-4, 6, 11, 12, and 16-19, insofar as the claims are drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing an apoptosis assay system.

Species C, claim(s) 1-4, 6, 11, 12, and 16-19, insofar as the claims are drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing a cell proliferation assay system.

Species D, claim(s) 1-4, 6, 11, 12, and 16-19, insofar as the claims are drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing an angiogenesis assay system.

Species E, claim(s) 1-4, 6, 11, 12, and 16-19, insofar as the claims are drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing a hypoxic induction assay system.

Species F, claim(s) 1-4 , 8-12, and 16-19, insofar as the claims are drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing an expression assay system.

Group II:

Species A, claims 13-15 and 20-22, insofar as the claims are drawn to a method for modulating a AXIN pathway of a cell, wherein said method comprises contacting a cell with an antibody that specifically binds to a MAX polypeptide.

Species B, claims 13-15 and 20-22, insofar as the claims are drawn to a method for modulating a AXIN pathway of a cell, wherein said method comprises contacting a cell with a non-antibody small molecule that specifically binds to a MAX polypeptide.

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The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is providing an assay system and contacting the assay system with a test agent to identify a candidate AXIN pathway-modulating agent.

The special technical feature of Group II is contacting a cell with a candidate modulator that specifically binds to a MAX polypeptide.

The special technical feature of Group III is contacting a cell with a candidate modulator that specifically binds to a nucleic acid molecule.

The special technical feature of Group IV is diagnosing a disease by measuring and comparing the expression of MAX.

Accordingly, Groups I-IV do not share the same or corresponding special technical feature so as to form a single general inventive concept under PCT Rules 12.1 and 13.2.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Group I.

The special technical feature of Species A is providing a binding assay system.

The special technical feature of Species B is providing an apoptosis assay system.

The special technical feature of Species C is providing a cell proliferation assay system.

The special technical feature of Species D is providing an angiogenesis assay system.

The special technical feature of Species E is providing a hypoxic induction assay system.

The special technical feature of Species F is providing an expression assay system.

Accordingly, Species A-F of the generic invention of claims 1-12 and 16-19 do not share the same or corresponding special technical feature so as to form a single general inventive concept under PCT Rules 12.1 and 13.2.

Group II.

The special technical feature of species (a) of Claims 13-15 and 20-22 is contacting a cell with a small molecule modulator that binds a MAX polypeptide.

The special technical feature of species (b) of Claims 13-15 and 20-22 is contacting a cell with an antibody that binds a MAX polypeptide.

Accordingly, Species A and B of the generic invention of claims 13-15 and 20-22 do not share the same or corresponding special technical feature so as to form a single general inventive concept under PCT Rules 12.1 and 13.2.

Continuation of Box II Item 4:
1-5, 7, 11, 12, and 16-19, insofar as the claims are drawn to a method for identifying a candidate AXIN pathway modulating agent, where said method comprises providing a primary assay system, which is a binding assay system.

Continuation of B. FIELDS SEARCHED Item 3:

INTERNATIONAL SEARCH REPORT

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MEDLINE, WEST: screening candidate modulators; AXIN; MAX; modifier of AXIN; AXIN-binding protein; binding assay; inhibitor; antagonist; agonist; small molecule; defective signaling; AXIN-dependent signaling pathway; antibody; mouse model system; cell culture assay system; phenotypic change