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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: MODULATION OF ANGIOGENESIS BY A-BETA PEPTIDES

(57) Abstract: The present invention provides methods and compositions for treating diseases and pathological conditions or processes mediated by undesired and/or uncontrolled angiogenesis (characterized as "angiogenic diseases") by increasing the *in vivo* concentration of the A β peptide, or biologically active fragments or variants of the A β peptide, within a patient suffering from such diseases, conditions, or processes. The present invention also concerns diagnostic methods and kits for detection and measurement of anti-angiogenic A β peptide activity in biological fluids and tissues. Such diagnostic methods and kits can be utilized to screen compounds for potential therapeutic activity in the treatment of Alzheimer's disease.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/27040

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A01N 37/18; A61K 38/00

US CL : 514/2

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. : 514/2

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	WO 94/10569 A1 (SCHENK et al) 11 May 1994 (11.05.1994), see whole document.	1-5, 10-14, 16-27
A	TARKOWSKI et al. Increased intrathecal levels of the angiogenic factors VEGF and TGF-beta in Alzheimer's disease and vascular dementia. Neurobiology of Aging. 2002, Vol. 23, pages 237-243.	1-5, 10-14, 16-27
X	PARIS et al. Soluble beta-amyloid peptides mediate vasoactivity via activation of a pro-inflammatory pathway. Neurobiology of Aging. 2000, Vol. 21, pages 183-197,	1-5
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A	especially page 184, see entire document.	10-14, 16-27

☐ 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	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

27 February 2003 (27.02.2003)

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Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/27040

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.: 1-5, 10-14, 16-27 (SEQ ID NOs: 1-3)
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.

INTERNATIONAL SEARCH REPORT

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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 searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-5, 10-14, 16-27, drawn to a method of preventing or alleviating the symptoms of an angiogenesis-mediated disease in a patient by administering A β peptide to the patient in vivo.

Group II, claim(s) 1, 6-10, 15, and 24-27, drawn to a method of preventing or alleviating the symptoms of an angiogenesis-mediated disease in a patient by administering cells that are genetically modified with a polynucleotide encoding A β peptide in vitro.

Group III, claim(s) 28-45 and 52-54, drawn to a method of identifying compounds that interfere with A β -induced angiogenesis inhibition using a biologically active amount of an A β peptide, an angiogenic agent and biological sample, and a kit for the testing.

Group IV, claim(s) 46-51 and 55-57, drawn to a method for identifying compounds that interfere with A β -induced anti-tumor activity using a biologically active amount of an A β peptide and tumor tissue, and a kit for the testing.

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 invention to be examined, the appropriate additional examination fees must be paid. The invention differs as follows:

Groups I-IV contain SEQ ID NOs: 1-3 and 7-11; (8 inventions for each group)

Groups I and II further contain cancer, arthritis, atherosclerosis, psoriasis, macular degeneration, or diabetic retinopathy. [(8 x 6) x 2 = 96 inventions]

Group III further contains arterial tissue, corneal tissue, endothelial tissue, umbilical cord tissue, or chorionic allantoic membrane (8x5 = 40); which further contains; Trophic factor, cytokine, VEGF, PDGF, or BFGF (40 x 5 = 200); which further contains in vitro or in vivo (200 x 2 = 400 inventions)

Group IV further contains in vitro or in vivo (8 x 2 = 16 inventions)

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: Group I encompasses a method of preventing or alleviating the symptoms of an angiogenesis-mediated disease in a patient by administering Abeta peptide to the patient. Groups II-IV are directed to different methods each method require specific technical feature other than the technique used in Group I. Further Groups I-IV contain different sequences set forth in SEQ ID NOs: 1-3 and 7-11, each differ at chemical structure and biological function; Furthermore, Groups I and II contain different diseases; Group III uses different tissues; Group IV contain in vitro an in vivo methods of testing. Moreover, the Abeta peptides were well-known in the art, as evidenced by Schenk et al (WO 94/10569). Thus, Groups I-IV lack a common technical feature. Further, 37 CFR 1.475 does not provide for multiple independent products, methods of manufacture and methods of use. Therefore, the inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1.

Applicants protest to pay two additional search fees for SEQ ID NO: 2 and 3 is acknowledged and is found persuasive. SEQ ID NO: 2 and 3 will be rejoined with Group I and SEQ ID NO: 1.

The protest to rejoin claims 1-57 is not found persuasive because in view of 37 CFR 1.475, one product, one method of producing the product, and one method of using the product will be searched. As displayed by applicants' protest there are several methods of using the product (Abeta peptide). Thus, the protest is not found persuasive and the claims will not be rejoined with Group I.

INTERNATIONAL SEARCH REPORT

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Continuation of B. FIELDS SEARCHED Item 3:

WEST 2.1, STN

serach terms: Abeta peptide, beta amyloid, angiogenesis, protein therapy, polypeptide therapy, cancer