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(71) Applicant *(for all designated States except US)*: **THE JOHNS HOPKINS UNIVERSITY** [US/US]; 100 N. Charles Street, 5th Floor, Baltimore, MD 20201 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ZACK, Donald, J.** [US/US]; 3 Ruby Field Court, Baltimore, MD 21287 (US). **KAGEYAMA, Masaaki** [JP/US]; 6602 Bonnie Ridge Drive, Apt. T-1, Baltimore, MD 21209 (US).

(74) Agent: **KAGAN, Sarah, A.**; Banner & Witcoff, Ltd., 11th floor, 1001 G Street, N.W., Washington, DC 20001-4597 (US).

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Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
18 November 2004

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: NEURONAL GENE EXPRESSION PATTERNS

(57) Abstract: Neuronal cell death, as modeled by removal of serum or NGF from growth medium, is characterized by many changes in gene expression. Gene expression was compared before and after withdrawal of serum or NGF. These results provide clues to underlying molecular processes occurring during neuronal and photoreceptor degeneration, and provide direction for future cell-based studies.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/21729

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/00, 39/395; C07K 16/00, 16/18, 16/22, 16/40
US CL : 424/130.1, 135.1, 136.1, 514/2; 530/387.1, 388.1

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. : 424/130.1, 135.1, 136.1, 514/2; 530/387.1, 388.1

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	US 6,323, 218 B1 (BUSH et al.) 27 November 2001 (27.11.1998), entire document.	1-9
A	LEVIN, L.A. et al. Expression of Ceruloplasmin in the Retina: Induction after Optic Nerve Crush. Investigative Ophthalmology & Visual Science. January 1998, Vol. 39, No. 1, pages 157-163, entire document.	1-9
A	CONNOR, J.R. et al. Ceruloplasmin levels in the human superior temporal gyrus in aging and Alzheimer's disease. Neurosci. Lett. 03 September 1993, Vol. 159, No. 1-2, pages 88-90, entire document.	1-9
A	CHEN, L. et al. Increased expression of ceruloplasmin in the retina following photic injury. Molecular Vision, 2003, Vol. 9, pages 151-158, entire document.	1-9
A	MIYAHARA, T. et al. Gene Microarray Analysis of Experimental Glaucomatous Retina from Cynomologous Monkey. Invest Ophthalmol Vis Sci. October 2003, Vol. 44, No. 10, pages 4347-4356, entire document.	1-9

☐ 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
21 May 2004 (21.05.2004)	01 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 T. Roberts for Christopher J Nichols, Ph.D. Telephone No. (571) 272-1600

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/21729

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.: 1-9

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 1, claim(s) 1-9, drawn to a method of inhibiting neuronal cell death comprising administering to a subject in need thereof an effective amount of an **antibody variable region**.

Group 2, claim(s) 10 and 12-19 (each in part), drawn to a method of preventing neuronal cell death comprising administering to a subject in need thereof an effective amount of a **nucleic acid molecule**.

Group 3, claim(s) 11 and 12-19 (each in part), drawn to a method of preventing neuronal cell death comprising administering to a subject in need thereof an effective amount of a **purified human neuronal marker protein**.

Group 4, claim(s) 20-28, drawn to a method of identifying regions of neuronal cell death comprising administering to a patient an **antibody variable region**.

Group 5, claim(s) 29, drawn to a method of screening for neuronal cell death comprising contacting a body fluid collected from the patient with an **antibody variable region**.

Group 6, claim(s) 30-31, drawn to a method of promoting neuronal cell death comprising administering to a patient in need a **purified human neuronal marker protein**.

Group 7, claim(s) 32-33, drawn to a method of promoting neuronal cell death comprising administering to a patient in need a **nucleic acid molecule**.

Group 8, claim(s) 34, drawn to a method of screening for neuronal cell death comprising detecting a **neuronal marker protein**.

Group 9, claim(s) 35, drawn to a method of screening for neuronal cell death comprising detecting a **nucleic acid**.

Group 10, claim(s) 36-38 and 45-47, drawn to a method to identify candidate drugs for treating neuronal cell death comprising contacting cells which express one or more neuronal marker genes and determining expression of said one or more neuronal marker genes by **hybridization of mRNA**.

Group 11, claim(s) 39-44 and 48-53, drawn to a method to identify candidate drugs for treating neuronal cell death comprising contacting cells which express one or more neuronal marker genes and determining the amount of said one or more **neuronal marker proteins**.

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.

The species are as follows:

The following claim(s) are generic:

Group 1, Claim 1, all species listed therein.

Group 2, Claim 10, all species listed therein.

Group 3, Claim 11, all species listed therein.

Group 4, Claim 20, all species listed therein.

Group 5, Claim 29, all species listed therein.

Group 6, Claim 30, all species listed therein.

Group 7, Claim 32, all species listed therein.

Group 8, Claim 34, all species listed therein.

Group 9, Claim 35, all species listed therein.

Group 10, Claims 36 and 45, all species listed therein.

Group 11, Claims 39 and 48, all species listed therein.

Group 12, Claims 42 and 51, all species listed therein.

In order for more than one species to be examined, the appropriate additional examination fees must be paid.

Applicant is invited to select one species per generic claim listed per group elected. and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups 1-12 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:

Each group employs a different inventive concept, each not shared with the other. 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:
the species listed herein do not share a common structure or function.

In the absence of any response from the applicant, this Authority will establish the International Preliminary Examination Report based on the main invention.
The claims drawn to the main invention are as follows: Claims: 1-9

Continuation of B. FIELDS SEARCHED Item 3:
WEST (USPT, PGPUBS, EPO, JPO, DERWENT), STN (BIOSCIENCE), PUBMED (MEDLINE)
antibody, ceruloplasmin, ferroxidase, therapy, neuronal cell death, apoptosis, neucrosis