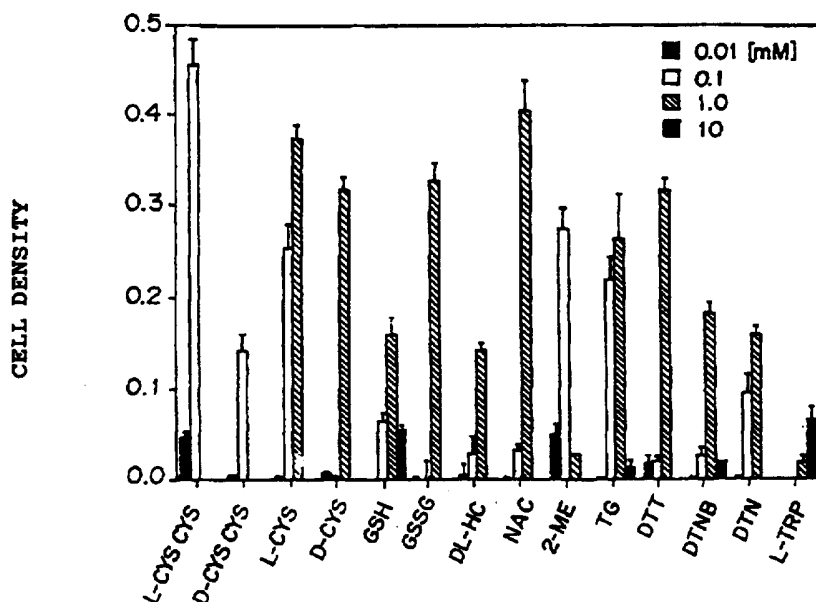




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 5/00, 5/06	A3	(11) International Publication Number: WO 96/05286 (43) International Publication Date: 22 February 1996 (22.02.96)
<p>(21) International Application Number: PCT/JP95/01581</p> <p>(22) International Filing Date: 9 August 1995 (09.08.95)</p> <p>(30) Priority Data: 6/192403 16 August 1994 (16.08.94) JP</p> <p>(71) Applicant: KABUSHIKI KAISHA FRONTIER [JP/JP]; 518, Waseda Tsurumaki-cho, Shinjuku-ku, Tokyo 169 (JP).</p> <p>(72) Inventors: NAMIKI, Hideo; Kabushiki Kaisha Frontier, 518, Waseda Tsurumaki-cho, Shinjuku-ku, Tokyo 169 (JP). KURITA, Takeshi; 404-5, Fujima, Kawagoe-shi, Saitama-ken 356 (JP).</p> <p>(74) Agents: ISHIKAWA, Yasuo et al.; Park Shiba Building, 4F, 17-11, Shiba 2-chome, Minato-ku, Tokyo 105 (JP).</p>	<p>(81) Designated States: European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</p> <p>(88) Date of publication of the international search report: 25 April 1996 (25.04.96)</p>	

(54) Title: CELL DEATH ACCELERATOR AND CELL DEATH INHIBITOR



(57) Abstract

A first embodiment of a cell culture system has a cell death accelerator comprising one or more cell death inducing substances, including serum albumin, hemoglobin, glycine and glutamic acid. In a second embodiment a cell death inhibitor comprises one or more kinds of cell death inhibiting substances which include mercapto group containing amino acids, other mercapto group containing compounds and tryptophan. In a third embodiment a cell death inhibitor comprises an inhibitor of RNA or protein synthesis, optionally augmented with a thiol. The system can be applied to selectively induce death of cultured cells, such as neoplastic cell lines, or to inhibit death of other cells, such as neoplastic cell lines or non-neoplastic cells such as brain cells.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgystan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

INTERNATIONAL SEARCH REPORT

International Application No

PC1/JP 95/01581

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N5/00 C12N5/06

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 6 C12N

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.
O, X	ZOOLOGICAL SCIENCE : SIXTY-FOURTH ANNUAL MEETING OF THE ZOOLOGICAL SOCIETY OF JAPAN, OKINAWA, JAPAN, NOVEMBER 20-23, 1993., vol. 10(supplement), 15 November 1993 HIROSHIMA, JAPAN, page 157 KURITA T; NAMIKI H 'Serum-induced cell death was rescued by thiols' see the abstract --- -/--	1-5, 7-9, 13-17, 19-23, 25, 26

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

23 January 1996

Date of mailing of the international search report

22 February 1996

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

Cupido, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 95/01581

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 9227 Derwent Publications Ltd., London, GB; Class B04, AN 92-223239 & JP,A,04 148 679 (KURITA T) , 21 May 1992 cited in the application see abstract ---	1,4-6, 13,16-20
X	ZOOLOGICAL SCIENCE, vol. 10, no. 3, 15 June 1993 HIROSHIMA, JAPAN, pages 431-438, T.KURITA AND H.NAMIKI 'Serum induced cell death' cited in the application see the whole document ---	10-12,27
A	EP,A,0 295 432 (BEHRINGWERKE AG) 21 December 1988 see the whole document ---	1-3
P,X	JOURNAL OF CELLULAR PHYSIOLOGY, vol. 161, no. 1, October 1994 pages 63-70, T.KURITA AND H.NAMIKI 'Apoptotic cell death induced by serum and its prevention by thiols' see the whole document -----	1-26

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP 95/01581

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.: 13-18, 27
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 13-18 and 27 in so far as an in vivo method is concerned 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 composition.
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.:

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

PL /JP 95/01581

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0295432	21-12-88	DE-A- 3717029 JP-A- 63313578	15-12-88 21-12-88
