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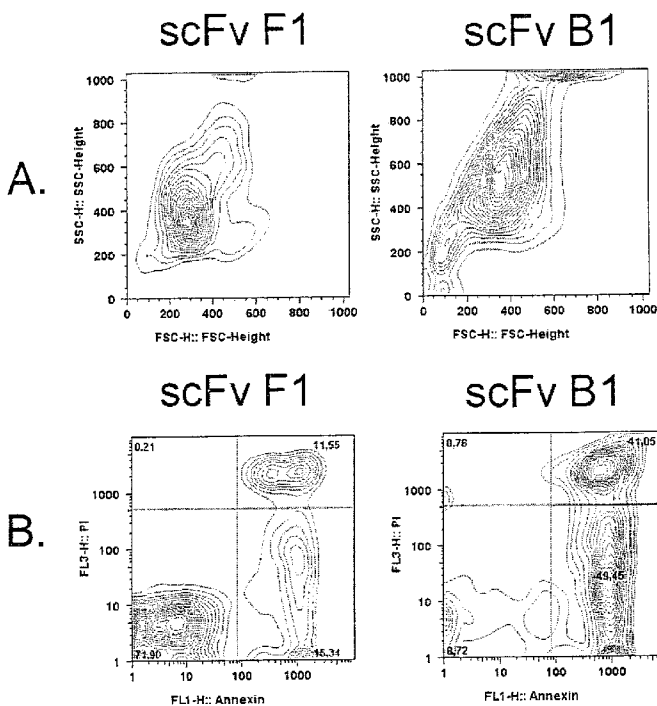
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[Continued on next page]

(54) Title: BIOLOGICAL MATERIALS AND USES THEREOF



(57) Abstract: The invention provides binding molecules, including antibody molecules which selectively bind to a cell surface antigen of a target cell, and wherein the binding molecules, on binding the cell surface antigen, induce apoptosis of the target cell. There is also provided methods of and pharmaceutical compositions for apoptosis induction and uses thereof.



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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) C07K		
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) EPO-Internal, BIOSIS, WPI Data, EMBASE		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	NAGY ZOLTAN A ET AL: "Fully human, HLA-DR-specific monoclonal antibodies efficiently induce programmed death of malignant lymphoid cells" NATURE MEDICINE, vol. 8, no. 8, August 2002 (2002-08), pages 801-807, XP002432676 ISSN: 1078-8956 abstract	1,2,4,6, 7,10-18, 20,22-31
X	page 803 ----- -/--	3,5, 8-19, 22-31
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> 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 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	Date of mailing of the international search report	
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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 Wagner, René	

INTERNATIONAL SEARCH REPORT

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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.
X	<p>US 2001/053360 A1 (VIDOVIC DAMIR [US] ET AL) 20 December 2001 (2001-12-20)</p> <p>paragraph [0114] paragraph [0115] paragraph [0125] paragraph [0135]</p> <p>-----</p>	3,5, 8-19, 22-31
X	<p>VIDOVIC D ET AL: "SELECTIVE APOPTOSIS OF NEOPLASTIC CELLS BY THE HLA-DR-SPECIFIC MONOCLONAL ANTIBODY" CANCER LETTERS, NEW YORK, NY, US, vol. 128, no. 2, 19 June 1998 (1998-06-19), pages 127-135, XP000857331 ISSN: 0304-3835 page 130</p> <p>-----</p>	3,5, 8-19, 22-31
A	<p>BUDAGYAN V M ET AL: "Anti-ICAM-1 mAb inhibits apoptosis of thymocytes induced by human thymic stromal cells (HTSC) line" TISSUE ANTIGENS, vol. 48, no. 4-2, 1996, page 359, XP009083145 & 6TH INTERNATIONAL WORKSHOP AND CONFERENCE ON HUMAN LEUKOCYTE DIFFERENTIATION ANTIGENS; KOBE, JAPAN; NOVEMBER 10-14, 1996 ISSN: 0001-2815 abstract</p> <p>-----</p>	1,2,4,6, 7,10-18, 20,22-31
A	<p>ZEN KATSUHIRO ET AL: "Monocyte-derived macrophages prime peripheral T cells of undergo apoptosis by cell-cell contact via ICAM-1/LFA-1-dependent mechanism" IMMUNOBIOLOGY, vol. 195, no. 3, 1996, pages 323-333, XP009083416 ISSN: 0171-2985 figure 6</p> <p>-----</p>	1,2,4,6, 7,10-18, 20,22-31
A	<p>NIEDA M ET AL: "Dendritic cells rapidly undergo apoptosis in vitro following culture with activated CD4+ Valpha24 natural killer T cells expressing CD40L" IMMUNOLOGY, BLACKWELL PUBLISHING, OXFORD, GB, vol. 102, no. 2, February 2001 (2001-02), pages 137-145, XP002364637 ISSN: 0019-2805 figure 5</p> <p>-----</p>	1,2,4,6, 7,10-18, 20,22-31
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/012065

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>YOSHIDA AYAKO ET AL: "Activated monocytes induce human retinal pigment epithelial cell apoptosis through caspase-3 activation." LABORATORY INVESTIGATION, vol. 83, no. 8, August 2003 (2003-08), pages 1117-1129, XP002432677 ISSN: 0023-6837 page 1120</p>	1,2,4,6, 7,10-18, 20,22-31
A	<p>DOYLE IRIS S ET AL: "Specific blockade by CD54 and MHC II of CD40-mediated signaling for B cell proliferation and survival" EXPERIMENTAL CELL RESEARCH, vol. 265, no. 2, 1 May 2001 (2001-05-01), pages 312-318, XP002432678 ISSN: 0014-4827 the whole document</p>	1,2,4,6, 7,10-18, 20,22-31
P,X	<p>FRANSSON JOHAN ET AL: "Rapid induction of apoptosis in B-cell lymphoma by functionally isolated human antibodies" INTERNATIONAL JOURNAL OF CANCER, vol. 119, no. 2, July 2006 (2006-07), pages 349-358, XP002432679 ISSN: 0020-7136 the whole document</p>	1,2,4,6, 7,10-18, 20,22-31
P,A	<p>WANG SHIXUAN ET AL: "Effect of an anti-cd54 (ICAM-1) monoclonal antibody (UV3) on the growth of human uveal melanoma cells transplanted heterotopically and orthotopically in SCID mice" INTERNATIONAL JOURNAL OF CANCER, vol. 118, no. 4, February 2006 (2006-02), pages 932-941, XP002432680 ISSN: 0020-7136 the whole document</p>	1,2,4,6, 7,10-18, 20,22-31
A	<p>SMALLSHAW JOAN E ET AL: "The generation and anti-myeloma activity of a chimeric anti-CD54 antibody, cUV3" JOURNAL OF IMMUNOTHERAPY, vol. 27, no. 6, November 2004 (2004-11), pages 419-424, XP009083506 ISSN: 1524-9557 the whole document</p>	1,2,4,6, 7,10-18, 20,22-31
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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2006/012065

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	<p>COLEMAN ELAINE J ET AL: "The Fc portion of UV3, an anti-CD54 monoclonal antibody, is critical for its antitumor activity in SCID mice with human multiple myeloma or lymphoma cell lines." JOURNAL OF IMMUNOTHERAPY (HAGERSTOWN, MD. : 1997) 2006 SEP-OCT, vol. 29, no. 5, September 2006 (2006-09), pages 489-498, XP009083509 ISSN: 1524-9557 the whole document -----</p>	1,2,4,6, 7,10-18, 20,22-31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2006/012065

Box II Observations where certain claims were found unsearchable (Continuation of item 2 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.: 32-47
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-3,24 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 compound/composition.
2. Claims Nos.: 32-47
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:
see FURTHER INFORMATION sheet PCT/ISA/210
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 III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional 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.:
1,2, 3 (in part), 5(in part), 8, 10-18 (in part), 19,20,22-31 (in part)
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-2,4,6-7,10-18 (in part),20,22-31 (in part)

Methods for inducing apoptosis using anti-ICAM-1 antibodies, anti-ICAM-1 antibodies useful in the methods and therapeutic use of the anti-ICAM-1 antibodies.

2. claims: 3,5,8,9,10-18 (in part), 19, 22-31 (in part)

Methods for inducing apoptosis using anti HLA-DR/DP antibodies, anti-HLA-DR/DP antibodies useful in the methods and therapeutic use of the anti-HLA-DR/DP antibodies.

3. claims: 3,5,8,9,10-18 (in part),21,22-31 (in part)

Methods for inducing apoptosis using anti-surface IgM antibodies, anti-surface IgM antibodies useful in the methods and therapeutic use of the anti-surface IgM antibodies

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 1-3,24 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 compound/composition.

Continuation of Box II.2

Claims Nos.: 32-47

1. Claims 32-37 and 38-43 are directed respectively to an in vitro and an in vivo method of inducing apoptosis, similar to the methods of claims 1-3, but in which the antibodies are indirectly defined by referring to claims 4-21. In claims 4-21 the antibodies are defined by the use in methods 1-3, which comprise the same steps as claims 4-21. It is not clear to which extent the scope of the methods of claims 32-43 might differ from the scope of claims 1-3. If the scope does not differ said claims are redundant, if however the scope differs, the differences do not appear. Therefore the scope of claims 32-43 is considered to be unclear (Article 6 PCT) to a degree for which a meaningful search is not possible. Therefore claims 32-43 were not searched. .

2. Claims 44-47 are not clear (Article 6 PCT) because they are defined by referring to the examples and figures in general. As the features defining the scope of these claims are totally unclear, a meaningful search is not possible for said claims.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2006/012065

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2001053360	A1	NONE	
