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(54) Title: ALPHA-FETOPROTEIN IMM31 ANTIBODIES AND FUSION PROTEINS AND METHODS OF USE THEREOF

(57) Abstract: The present invention provides humanized, chimeric and human anti-alpha-fetoprotein antibodies, fusion proteins, and fragments thereof. The antibodies, fusion proteins, and fragments thereof, as well as combinations with other suitable antibodies, are useful for the treatment and diagnosis of hepatocellular carcinoma, hepatoblastoma, germ cell tumors carcinoma and other AFP-producing tumors.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/03325

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	C07K16/18	C07K16/46	A61K51/10	A61K47/48	A61K39/395
	G01N33/573	G01N33/574	C12N15/13	C12N15/62	C12N15/79
	C12N5/10	A61P35/00	C12Q1/68		

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 7	C07K A61K

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, EMBASE, CHEM ABS Data, WPI Data, PAJ, Sequence Search	

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Z. QU ET AL.: "Humanization of Immu31, an alpha-fetoprotein-specific antibody." CLINICAL CANCER RESEARCH, vol. 5, no. 10 suppl., October 1999 (1999-10), pages 3095s-3100s, XP001154527 USA the whole document	1-4, 9-17, 19, 21, 22, 25-27, 36, 37, 73, 74, 77-80, 83-85, 130, 144-147, 149-157, 219-221

<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.
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* 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 document but 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	Date of mailing of the international search report
29 March 2004	12 JUL 2004

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 Nooij, F
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/03325

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 612 016 A (GRIFFITHS ET AL.) 18 March 1997 (1997-03-18) examples columns 11-12 -----	1,22, 25-29, 33-37, 48,49, 53-56, 71-74, 80, 83-90, 94,95, 105-110, 130, 154-157, 219-221
X	WO 96/37516 A (STRAHILEVITZ) 28 November 1996 (1996-11-28) example 3 -----	1,21,22, 38-40, 58,71, 72,80, 95-98, 131,154, 155
X	D. GOLDENBERG: "Targeted therapy of cancer with radiolabeled antibodies." THE JOURNAL OF NUCLEAR MEDICINE, vol. 43, no. 5, May 2002 (2002-05), pages 693-713, XP002275000 New York, NY, USA abstract figure 1 tables 2,4 page 708, left-hand column, line 8 - line 14 -----	1,3,22, 25-27, 71-74, 80, 83-85, 130,131, 139,154, 155
X	S. DRESEL ET AL.: "Detection of hepatocellular carcinoma with a new alpha-fetoprotein antibody imaging kit." JOURNAL OF CLINICAL ONCOLOGY, vol. 15, no. 7, July 1997 (1997-07), pages 2683-2690, XP008026812 New York, NY, USA abstract ----- -/--	1,2,21, 22, 25-27, 36,73, 74,80, 83-85, 95,105, 106,130, 154,155, 219-221

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/03325

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.: 5-7, 18, 20, 46, 47, 66, 69, 70, 102, 148
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
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:

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.:
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.:
1-4, 8-17, 19, 21-45 all completely 71-74, 77-101, 103-111, 130, 131
136-140, 142-147, 149-157 all partially 219-225 all completely

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

Continuation of Box I.1

Although claims 71 and 72 (both completely), 80-101 and 103-111 (all partially), 131, 136-140, 142 and 143 (all completely) and 154-157 (all partially) are directed to a method of treatment of the human/animal body, and although claims 73 and 74 (both completely), 80-101 and 103-111 (all partially), 130, 144-147 and 149-153 (all completely), 154-157 (all partially) and 219-223 (all completely) are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: 5-7,18,20,46,47,66,69,70,102,148

Since claims 5-7, 18, 20, 46, 47, 66, 69, 70, 102 and 148 were not present in the set of claims, they could not be searched

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-4, 8-17, 19, 21-45, 48-58 (all completely), 71-74, 77-101, 103-111, 130, 131, 136-140, 142-147, 149-157 (all partially), 219-225 (all completely)

A monospecific monoclonal antibody against alpha-fetoprotein. Also fragments and immunoconjugates thereof. Its therapeutic and diagnostic uses.

2. claims: 59-65, 67, 68 (all completely), 71-74 (all partially), 75, 77 (both completely), 77-101 and 103-111 (both partially), 112-114 (all completely), 130, 131, 136-140, 142-147 and 149-157 (all partially) and 158-218 (all completely)

Multispecific antibody or antibody fusion protein, comprising at least one binding site specific for alpha-fetoprotein. Also fragments thereof. Its therapeutic and diagnostic uses.

3. claims: 115-129, 132-135 and 141 (all completely), 143 and 154-157 (all partially)

Method of treating a malignancy in a subject comprising administering an antibody or fragment thereof, or an antibody fusion protein or a fragment thereof, comprising at least 2 monoclonal antibodies, at least one of which has a specificity for alpha-fetoprotein.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/03325

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