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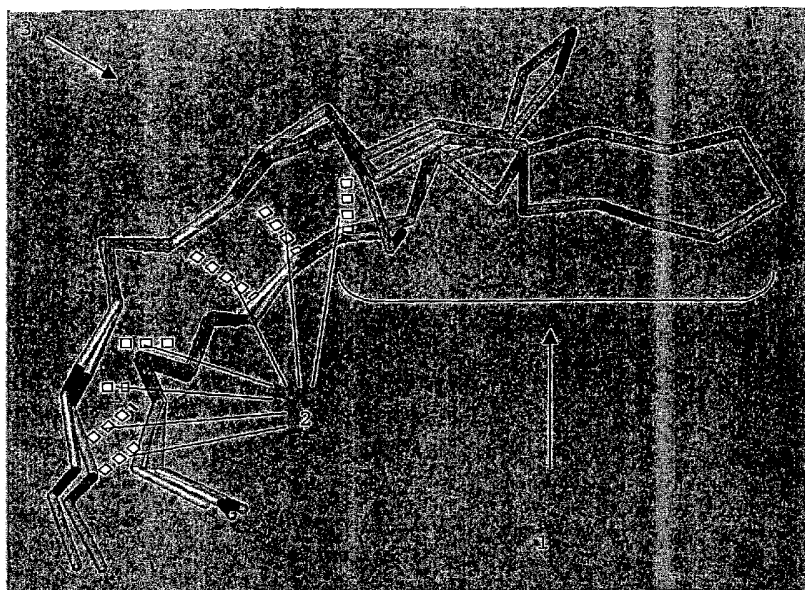
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[Continued on next page]

(54) Title: METHOD FOR DISPLAYING LOOPS FROM IMMUNOGLOBULIN DOMAINS IN DIFFERENT CONTEXTS



(57) Abstract: The present invention is related to an isolated polypeptide micro-scaffold displaying immunoglobulin CDR2 or CDR3 polypeptide sequences, comprising a CDR2 or CDR3 polypeptide sequence interconnecting fragments of the adjacent framework polypeptide sequences, which are arranged to form two anti-parallel β -strands. The present invention is further related to a method to search, select or screen for immunoglobulin CDR2 or CDR3 polypeptide sequences that bind to a given antigen or mixture of antigens, comprising the steps of: Creating a CDR library with the method of claim 13 from the genetic information of an individual or group of individuals; Select a CDR, which binds to said antigen or mixture of antigens.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/BE 02/00189

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12Q1/68 G01N33/68 A61K39/395				
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 G01N				
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, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	BILLETTA, R. ET ZANETTI, M.: "Antigenicity and immunogenicity of antigenized antibodies. Studies on B and T cells." INTERNATIONAL REVIEWS OF IMMUNOLOGY, vol. 10, no. 2-3, 1993, pages 251-263, XP009010620 Switzerland	1,2,4,5, 7,8,12		
Y	the whole document --- -/--	1-18		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> <input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. </td> <td style="width: 50%; border: none;"> <input checked="" type="checkbox"/> Patent family members are listed in annex. </td> </tr> </table>			<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.
<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.			
° Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> <ul style="list-style-type: none"> *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 </td> <td style="width: 50%; border: none;"> <ul style="list-style-type: none"> *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 </td> </tr> </table>			<ul style="list-style-type: none"> *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 	<ul style="list-style-type: none"> *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
<ul style="list-style-type: none"> *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 	<ul style="list-style-type: none"> *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 <p style="text-align: center; font-size: 1.2em;">27 May 2003</p>		Date of mailing of the international search report <p style="text-align: center; font-size: 1.2em;">04/06/2003</p>		
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 <p style="text-align: center; font-size: 1.2em;">Moreno de Vega, C</p>		

INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 02/00189

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZHAO, B ET AL: "A paradigm for drug discovery using a conformation from the crystal structure of a presentation scaffold" NATURE STRUCTURAL BIOLOGY, vol. 2, no. 12, December 1995 (1995-12), pages 1131-1137, XP009010617 USA the whole document	1-18
X	KOIDE A ET AL: "THE FIBRONECTIN TYPE III DOMAIN AS A SCAFFOLD FOR NOVEL BINDING PROTEINS" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 284, 1998, pages 1141-1151, XP002944100 ISSN: 0022-2836 the whole document	1,2,4-15
Y	the whole document	1-18
Y	WO 98 32845 A (BIOINVENT INTERNATIONAL AB) 30 July 1998 (1998-07-30) the whole document	1-18
Y	SODERLIND ESKIL ET AL: "Recombining germline-derived CDR sequences for creating diverse single-framework antibody libraries." NATURE BIOTECHNOLOGY, vol. 18, no. 8, August 2000 (2000-08), pages 852-856, XP009010618 ISSN: 1087-0156 the whole document	1-18
X	WO 00 34784 A (PHYLOS, INC) 15 June 2000 (2000-06-15) the whole document	1,2,4-15
Y	the whole document	1-18
X	WO 01 49713 A (ENTE PER LE NUOVE TECNOLOGIE) 12 July 2001 (2001-07-12)	1,2,4-15
Y	page 5, line 5 -page 16, line 3 page 18, line 3 -page 33	1-18
X	DESIDERIO, A. ET AL: "A semi-synthetic repertoire of intrinsically stable antibody fragments derived from a single-framework scaffold" J. MOL. BIOL., no. 310, 2001, pages 603-615, XP001152504 the whole document	1,2,4-15
Y	the whole document	1-18
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/BE 02/00189

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NUTTALL, S.D. ET AL: "Isolation of the antigen receptor from wobbegong sharks, and use as a scaffold for the display of protein loop libraries" MOLECULAR IMMUNOLOGY, no. 38, 2001, pages 313-326, XP001152503	1,2,4-15
Y	the whole document -----	1-18

INTERNATIONAL SEARCH REPORT

International application No.
PCT/BE 02/00189

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.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: **19**
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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 19

Present claim 19 relate to an extremely large number of possible methods with reference to CDR sequences defined by a method for their identification. In fact, the claim contain so many options that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claim impossible.

The applicant's attention is drawn to the fact that claims, or parts of 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/BE 02/00189

Patent document cited in search report	A	Publication date		Patent family member(s)	Publication date
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				CA 2395041 A1	12-07-2001
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				WO 0149713 A2	12-07-2001