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(54) Synthetic antibody phage libraries

(57) The invention provides comprising variant amino acids in CDRs of antibody variable domains. These polypeptides provide a source of great sequence diversity that can be used as a source for identifying novel antigen binding polypeptides. The invention also provides these polypeptides as fusion polypeptides to heterologous polypeptides such as at least a portion of phage or viral coat proteins, tags and linkers. Libraries comprising a plurality of these polypeptides are also provided. In addition, methods of and compositions for generating and using these polypeptides and libraries are provided.

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EUROPEAN SEARCH REPORT

Application Number
EP 10 01 1041

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	GARRARD & D J HENNER L J: "Selection of an anti-IGF-1 Fab from a Fab phage library created by mutagenesis of multiple CDR loops", GENE, ELSEVIER, AMSTERDAM, NL, vol. 128, 1 January 1993 (1993-01-01), pages 103-109, XP025516241, ISSN: 0378-1119, DOI: 10.1016/0378-1119(93)90160-5 * page 104, column 1, paragraph 2 - page 105; tables 1-4 *	1-36	INV. C07K16/22 C07K16/32 C07K16/42 C07K16/00 C40B40/10
A	PINI A ET AL: "Design and use of a phage display library. Human antibodies with subnanomolar affinity against a marker of angiogenesis eluted from a two-dimensional gel", JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, US, vol. 273, no. 34, 21 August 1998 (1998-08-21), pages 21769-21776, XP002124781, ISSN: 0021-9258, DOI: 10.1074/JBC.273.34.21769 * page 21770, column 1 *	1-36	TECHNICAL FIELDS SEARCHED (IPC) C07K C40B
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~~The present search report has been drawn up for all claims~~

Place of search	Date of completion of the search	Examiner
Munich	7 January 2013	Mabit, Hélène

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
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E : earlier patent document, but published on, or after the filing date
D : document cited in the application
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3

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DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	WU H ET AL: "STEPWISE IN VITRO AFFINITY MATURATION OF VITAXIN, AN ALPHAVBETA3-SPECIFIC HUMANIZED MAB", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, NATIONAL ACADEMY OF SCIENCES, US, vol. 95, 1 May 1998 (1998-05-01), pages 6037-6042, XP000918969, ISSN: 0027-8424, DOI: 10.1073/PNAS.95.11.6037 -----	1-36	
T	SIDHU S S ET AL: "Phage-displayed Antibody Libraries of Synthetic Heavy Chain Complementarity Determining Regions", JOURNAL OF MOLECULAR BIOLOGY, ACADEMIC PRESS, UNITED KINGDOM, vol. 338, no. 2, 23 April 2004 (2004-04-23), pages 299-310, XP004500301, ISSN: 0022-2836, DOI: 10.1016/J.JMB.2004.02.050 -----		TECHNICAL FIELDS SEARCHED (IPC)
T	FUH GERMAINE: "Synthetic antibodies as therapeutics", EXPERT OPINION ON BIOLOGICAL THERAPY, ASHLEY, LONDON, GB, vol. 7, no. 1, 1 January 2007 (2007-01-01) , pages 73-87, XP009099132, ISSN: 1471-2598 * page 76 - page 78 * -----		

~~The present search report has been drawn up for all claims~~

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Application Number
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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-36

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

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LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 10 01 1041

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-36

Subject-matter
- of claims 1-32, i.e. subject-matter related to a library comprising a plurality of polypeptides each comprising an heavy chain antibody variable domain, with a variant CDRH3, a variant CDRH2, and a variant CDRH1 as described in claim 1, and
- of claims 33-36, i.e. subject-matter related to a method comprising comprising a) constructing an expression vector comprising a polynucleotide sequence which encodes a light chain variable domain, a heavy chain variable domain or both of a source of antibody comprising at least 1 to all CDRs of the source antibody selected from the group consisting of CDRL1-3, and CDRH1-3, and b) mutaing all heavy chain CDRs of thew source antibody at all solvent accessible and highly diverse amino acid positions using a non random codon set, wherein at least 505 of the amino acids encoded by the non random codon set are target amino acids for that position in naturally occurring antibodies.

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2. claim: 37

A method for finding original binders from a library or finding improved binders from a library that was designated to improve affinity of a particular binding clone or group of clones, the method comprising:
contacting a plurality of polypeptides displayed on phage or phagemid particles with a target antigen labelled or fused with a tag molecule; and
separating the phage or phagemid particles that are bound to labelled targets from phage or phagemid that do not bind by (1) allowing binding to a molecule that binds the labelled target antigen for a period of 2-5 minutes and (2) eluting the bound particles.
