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(54) Title: ENHANCED PHAGE DISPLAY LIBRARY OF HUMAN VH FRAGMENTS AND METHODS FOR PRODUCING
SAME

(57) Abstract: Phage display libraries are taught in which the recombinant phage population displays a plurality of potential binding
fragments having preferred characteristics of solubility and/or intermolecular interaction. Also taught are methods of biasing display
libraries to produce variants which more closely approximate the preferred characteristics of the parental binding fragment.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
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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)
IPC 7 C07K 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)
BIOSIS, EMBASE, WPI Data, PAJ, EPO-Internal, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M. LAUWEREYS ET AL.: "Potent enzyme inhibitors derived from dromedary heavy-chain antibodies." THE EMBO JOURNAL, vol. 17, no. 13, 1 July 1998 (1998-07-01), pages 3512-3520, XP002136362 Oxford, GB cited in the application abstract page 3515, left-hand column, line 51 -right-hand column, line 7 figure 3 --- -/--	38-45, 75,84

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
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- *Z* document member of the same patent family

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INTERNATIONAL SEARCH REPORT

Inte. onal Application No

PCT/CA 00/01027

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>S. MUYLDERMANS ET AL.: "Sequence and structure of VH domain from naturally occurring camel heavy chain immunoglobulins lacking light chains." PROTEIN ENGINEERING, vol. 7, no. 9, September 1994 (1994-09), pages 1129-1135, XP000445081 Oxford, GB cited in the application abstract introduction</p>	38-45, 75,84
X	<p>Y. REITER ET AL.: "An antibody single-domain phage display library of a native heavy chain variable region: Isolation of functional single-domain VH molecules with a unique interface." JOURNAL OF MOLECULAR BIOLOGY, vol. 290, no. 3, 16 July 1999 (1999-07-16), pages 685-698, XP002165613 Oxford, GB cited in the application discussion figures abstract</p>	38, 40-42, 46,75,84
X	<p>J. DAVIES ET AL.: "Single antibody domains as small recognition units: design and in vitro antigen selection of camelized, human VH domains with improved protein stability." PROTEIN ENGINEERING, vol. 9, no. 6, 1996, pages 531-537, XP000971767 Oxford, GB cited in the application the whole document</p>	38, 40-42, 46,75,84
A	<p>WO 95 35374 A (M. DAN) 28 December 1995 (1995-12-28) cited in the application seq.id.no.13,14,21-23 claims 5,20</p>	1-88
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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.
A	<p>J. DE KRUIF ET AL.: "Selection and application of human single chain Fv antibody fragments from a semi-synthetic phage antibody display library with designed CDR3 regions." JOURNAL OF MOLECULAR BIOLOGY, vol. 248, no. 1, 1995, pages 97-105, XP000646544 Oxford, GB abstract introduction</p>	<p>29,30, 38, 40-42, 46,48,84</p>
A	<p>---- A. DESMYTER ET AL.: "Crystal structure of a camel single-domain VH antibody fragment in complex with lysozyme." NATURE STRUCTURAL BIOLOGY, vol. 3, no. 9, September 1996 (1996-09), pages 803-811, XP000990754 New York, NY, USA cited in the application the whole document</p>	<p>1-88</p>
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INTERNATIONAL SEARCH REPORT

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International Application No

PCT/CA 00/01027

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