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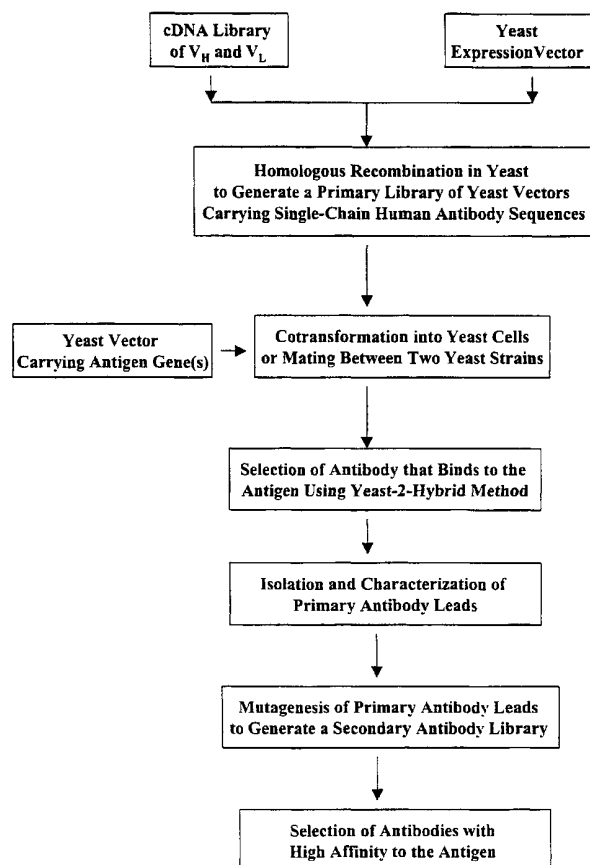
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[Continued on next page]

(54) Title: GENERATION OF LIBRARIES OF ANTIBODIES IN YEAST AND USES THEREOF



(57) Abstract: Compositions, kits and methods are provided for generating highly diverse libraries of proteins such as antibodies via homologous recombination *in vivo*, and screening these libraries against protein, peptide and nucleic acid targets using a two-hybrid method in yeast. The method for screening a library of tester fusion proteins against a target protein or peptide comprises: expressing a library of tester proteins in yeast cells, the tester fusion protein comprising a first polypeptide subunit whose sequence varies within the library, a second polypeptide subunit whose sequence varies within the library independently of the first polypeptide, and a linker peptide which links the first and second polypeptide subunits; expressing one or more target fusion proteins in the yeast cells expressing the tester proteins, each of the target fusion proteins comprising a target peptide or protein; and selecting those yeast cells in which a reporter gene is expressed, the expression of the reporter gene being activated by binding of the tester fusion protein to the target fusion protein.



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# INTERNATIONAL SEARCH REPORT

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**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C12N15/10 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)

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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, BIOSIS, CHEM ABS Data, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 28502 A (INVITROGEN CORP) 10 June 1999 (1999-06-10) page 15, line 18 -page 20, line 6 ---	1-143
X	VISINTIN MICHELA ET AL: "Selection of antibodies for intracellular function using a two-hybrid in vivo system" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 96, no. 21, 12 October 1999 (1999-10-12), pages 11723-11728, XP002143442 ISSN: 0027-8424 page 11728, left-hand column, paragraph 2 -right-hand column --- -/--	1-143



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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- \* & \* document member of the same patent family

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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	HOLTZ, A. E. ET AL.: "Yeast Hybrid Technologies: Chapter 5 (Mating-Based Yeast Two-Hybrid Screening)" 2000, EATON PUBLISHING, NATICK, MA XP001065214 page 89 -page 90, paragraph 2 -----	1-143
A	BENDIXEN C ET AL: "A yeast mating selection scheme for detection of protein-protein interaction" NUCLEIC ACIDS RES., vol. 22, no. 9, 1994, pages 1778-1779, XP002004038 page 1770, right-hand column, paragraph 1 -----	1-143
A	WANG PETER L: "Creating hybrid genes by homologous recombination." DISEASE MARKERS, vol. 16, no. 1-2, 2000, pages 3-13, XP001064283 Meeting on New Horizons for Phage Antibody Display Technology; Hull, England, UK; April 11-13, 2000 ISSN: 0278-0240 page 10, right-hand column, paragraph 2 -page 11 -----	1-143

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9928502	A	10-06-1999	WO 9928502 A1	10-06-1999
			AU 3587599 A	16-06-1999
			EP 1040201 A1	04-10-2000
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