



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US94/14106 (22) International Filing Date: 8 December 1994 (08.12.94) (30) Priority Data: 08/164,022 8 December 1993 (08.12.93) US 08/350,400 6 December 1994 (06.12.94) US (71) Applicant: GENZYME CORPORATION [US/US]; One Kendall Square, Cambridge, MA 02139 (US). (72) Inventors: BARSOMIAN, Gary; 68 Jewett Street, Georgetown, MA 01830 (US). COPELAND, Diane, P.; 7 Whittier Road, Billerica, MA 01821 (US). HILLHOUSE, Dana; Top floor, 33 Whitney Avenue, Beverly, MA 01915 (US). JOHNSON, Tracy; 136 Concord Avenue, Lexington, MA 02173 (US). (74) Agents: VINCENT, Matthew, P. et al.; Lahive & Cockfield, 60 State Street, Boston, MA 02109 (US).	(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 28 December 1995 (28.12.95)	
(54) Title: PROCESS FOR GENERATING SPECIFIC ANTIBODIES		
(57) Abstract The present invention relates to a method for generating an antibody which is specific for an immunorecessive epitope, and nucleic acid encoding the antibody. The subject method generally comprises the steps of generating a variegated display library of antibody variable regions, and selecting from the library those antibody variable regions which have a desired binding specificity for the immunorecessive epitope. The antibody variable regions used to generate the display library are cloned from an immunotolerance-derived antibody repertoire.		

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 94/14106

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/13 C07K16/00 C12N15/11

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 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JOURNAL OF MOLECULAR BIOLOGY, vol.222, 19 October 0 pages 581 - 597 J.D. MARKS ET AL. 'By-passing immunization. Human antibodies from V-gene libraries displayed on phage' *see the whole article* ---	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84
Y	BIOTECHNOLOGY, vol.11, pages 1145 - 1149 J.D. MARKS ET AL. 'Human antibody fragments specific for human blood group antigens from a phage display library' *see the whole article* ---	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84

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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- *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

6 Date of the actual completion of the international search: 10 July 1995

Date of mailing of the international search report: 04.12.95

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: Marie, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 94/14106

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NATURE, vol.352, 19 October 0 pages 624 - 628 *see the whole article* ---	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84
Y	JOURNAL OF IMMUNOLOGY, vol.151, no.5, pages 2839 - 2851 S. PORTOLANO ET AL. 'High affinity, thyroid-specific human autoantibodies displayed on the surface of filamentous phage using V genes similar to other autoantibodies' *see the whole article* ---	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84
Y	NUCLEIC ACIDS RESEARCH, vol.19, no.15, 19 October 0 pages 4133 - 4137 H.R. HOOGENBOOM ET AL. 'Multi-subunit proteins on the surface of filamentous phage: methodologie for displaying antibody (Fab) heavy and light chains' *see the whole article* ---	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84
Y	JOURNAL OF IMMUNOLOGY, vol.151, no.10, pages 5822 - 5839 M. SASANO ET AL. 'Molecular selection of human antibodies with an unconventional bacterial B cell antigen' *see the whole article* ---	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84
Y	MEDICAL HYPOTHESES, vol.17, pages 265 - 270 R.J. SHARPE ET AL. 'Neonatal tolerance increases efficacy of antisera production' *see the whole article* ---	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84
Y	BIOTECHNIQUES, vol.12, no.6, pages 842 - 847 C.V. WILLIAMS ET AL. 'Subtractive immunization techniques for the production of monoclonal antibodies to rare antigens' *see the whole article* -----	1-3,5,6, 11-31, 36-38, 44-49, 61-65, 79,82-84

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INTERNATIONAL SEARCH REPORT

International application No.

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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.:
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:

- claims 1-41, 44-69, 79-85: related to display libraries
- claims 42, 43, 70-78 : unrelated to display libraries

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.:

1-41, 44-69, 79-85

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.