

- [54] **RECOMBINANT IMMUNOGLOBIN PREPARATIONS**
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- [58] **Field of Search** 435/68, 172.3, 240, 435/253, 172.2, 317, 320; 260/112 B; 536/27; 935/11, 15, 27, 29, 73; 530/387, 388

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,444,878	4/1984	Paulus	435/188
4,512,922	4/1985	Jones et al.	435/68 X
4,518,584	5/1985	Mark et al.	435/172.3
4,704,362	11/1987	Itakura et al.	435/172.3 X

FOREIGN PATENT DOCUMENTS

0057107	8/1982	European Pat. Off.	.
0073656	8/1982	European Pat. Off. 435/172.3
0068763	1/1983	European Pat. Off.	.
0120694	10/1984	European Pat. Off.	.

OTHER PUBLICATIONS

- Dolby, T. W. et al. *Proc. Natl. Acad. Sci.*, vol. 77, (10) pp. 6027-6031, 1980.
- Rice, D. et al. *Proc. Natl. Acad. Sci.* vol. 79 pp. 7862-7865, 1982.
- Accolla, R. S. et al., *Proc. Natl. Acad. Sci.*, vol. 77, (1) pp. 563-566, 1980.
- Raso, V. et al., *Cancer Res.*, vol. 41, pp. 2073-2078, 1981.

- Nisonoff, A. et al., *Arch. Biochem. Biophys.*, vol. 93, pp. 460-462, 1960.
- Glennie, M. J. et al., *Nature*, vol. 295, pp. 712-714, 1982.
- Eisen, H. N., *Immunology*, Harper & Row, Publishers, pp. 415 and 428-436, 1974.
- Hozumi, N. et al. *Nuc Acids Res.* vol. 5(6) pp. 1779-1799, Chem. Abst. 89:87928t, 1978.
- Wetzel, R. et al. *Gene*, vol. 16, pp. 63-71, 1981.
- Williams et al., *Science*, vol. 215, pp. 687-689, 1982.
- Falkner, F. G. et al., *Nature*, vol. 298, pp. 286-288, 1982.
- Boss et al. Hamer et al., Ed. "Gene Expressions-Proc. Cetus-UCLA Symposium . . . Mar. 26-Apr. 1, 1983" pp. 513-522.
- Amster et al., "Nucleic Acid Research" 8(9): 2055-2065 (1980).
- DeBoer et al., Rodriguez et al., Ed. "Promoters" 462-481 (1982).
- Gough, "Tibs" 6(8): 203-205 (Aug. 1981).
- Morrison, "J. of Immunology" 123(2): 793-800 (Aug. 1979).
- Kohler "P.N.A.S. USA" 77(4): 2197-2199 (Apr. 1980).
- Thomas M. Roberts, *Promoters*, Rodriguez et al., Eds. (1982), pp. 452-461.
- Kemp et al., "Proc. Natl. Acad. Sci. USA" 78(7): 4520-4524 (Jul. 1981).
- Valle et al., "Nature" 300:71-74 (4 Nov. 1982).
- Microbiology 3rd ed., Harper Int. Ed. 338-379 (1980).
- Hitzeman et al. *Science* 219: 620-625 (1983).
- Mercereau-Puijalon et al., in "Expression of Eukaryotic Viral and Cellular Genes" Pettersson et al. (ED.) 295-303 (1981) Academic Pr.
- Primary Examiner*—Jayme Huleatt

(List continued on next page.)

[57] **ABSTRACT**

Altered and native immunoglobulins, including constant-variable region chimeras, are prepared in recombinant cell culture. The immunoglobulins contain variable regions which are immunologically capable of binding predetermined antigens. Methods are provided for re-folding directly expressed immunoglobulins into immunologically active form.

7 Claims, 15 Drawing Sheets

OTHER PUBLICATIONS

Keshet et al. Nucleic Acids Res. 9(1): 19-30 (1981).
Taniguchi et al., Proc. Natl. Acad. Sci. USA, 77(9):
5230-5233 (1980).
Ohsuye et al., Nucleic Acids Res. 11(5): 1283-1295
(1983).

Kadonaga et al., J. Biol. Chem. 259(4): 2149-2154
(1984).
Maniatis, T. "Molecular Cloning" p. 433 (Sep. 1985).
Fujisawa Y. et al. "Nucleic Acids Res." 11(11):
3581-3591 (1983).
Roberts, T. M. in "Promoters Structures and Function"
Rodriguez, R. L. (ED.) 452-461 (1982).

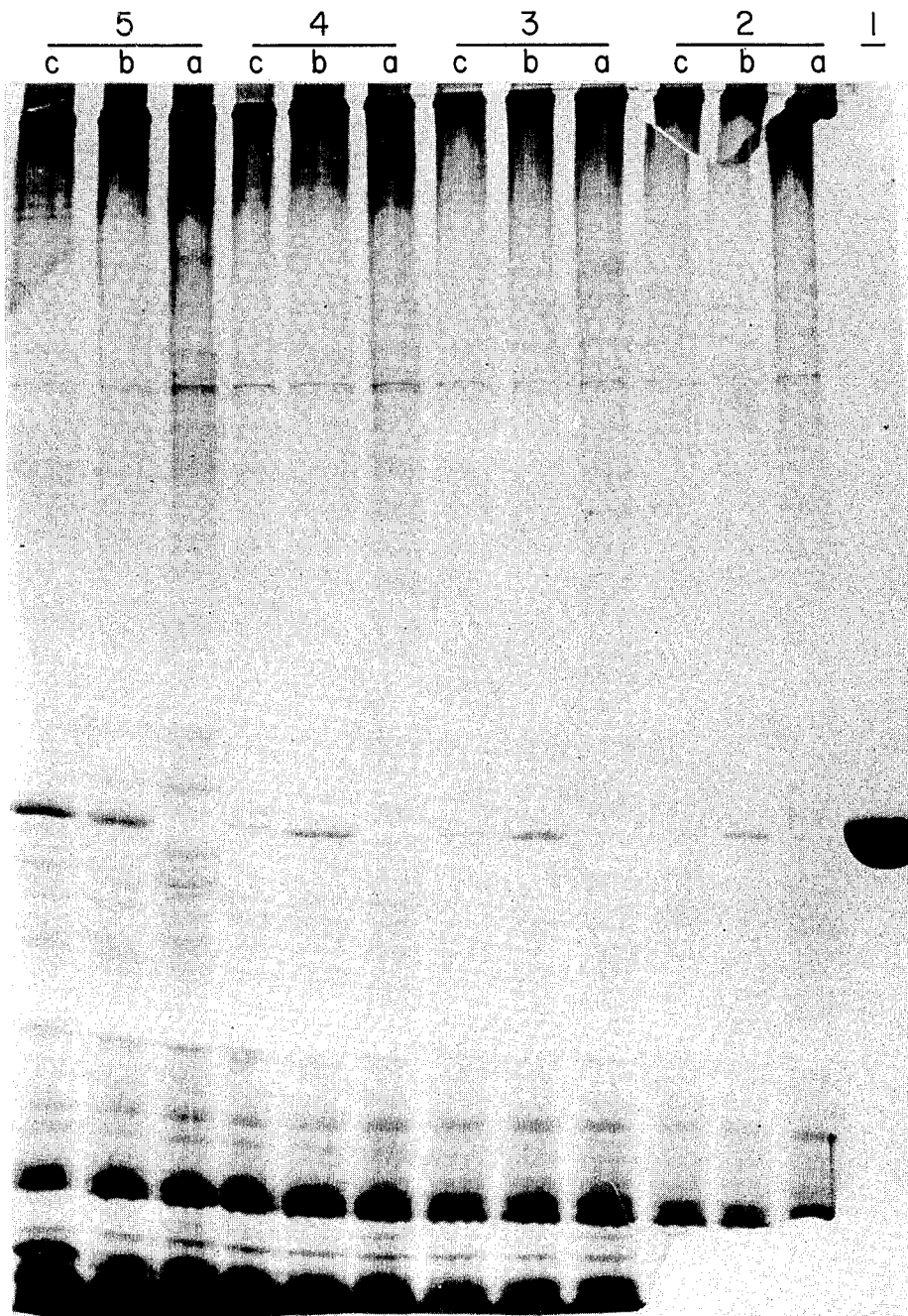
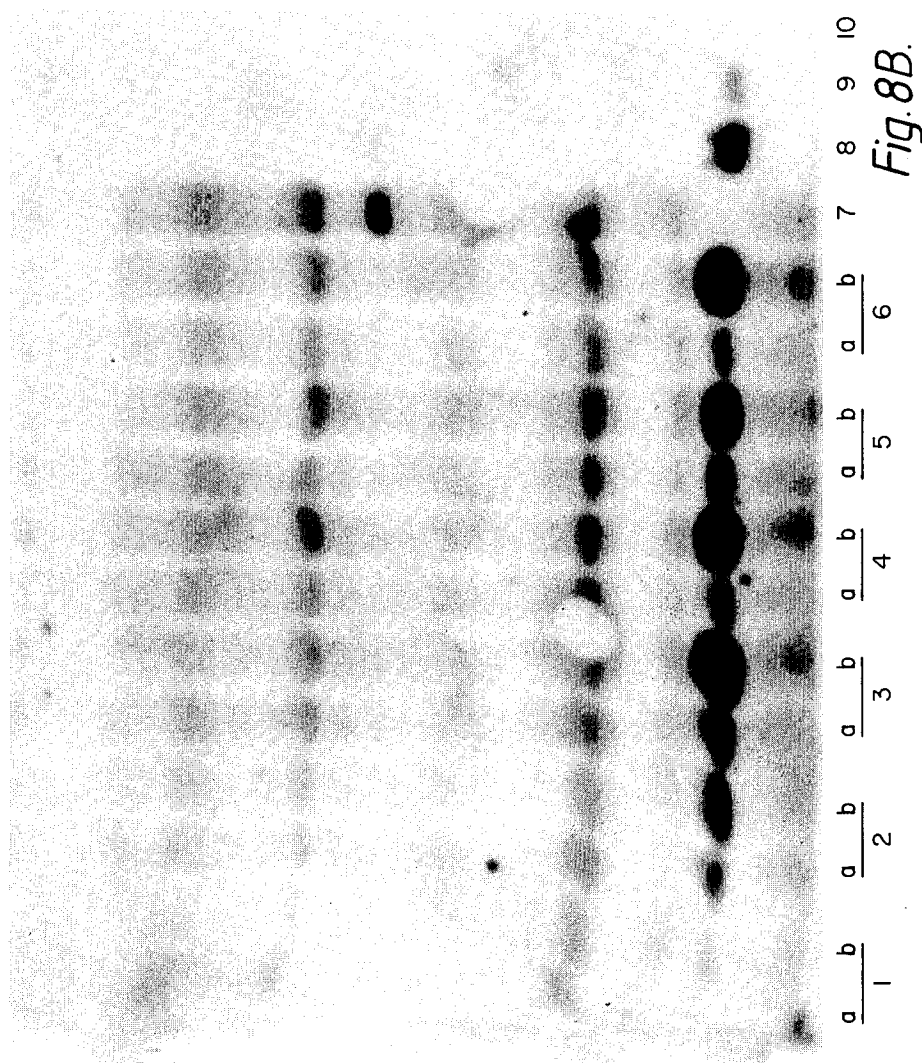
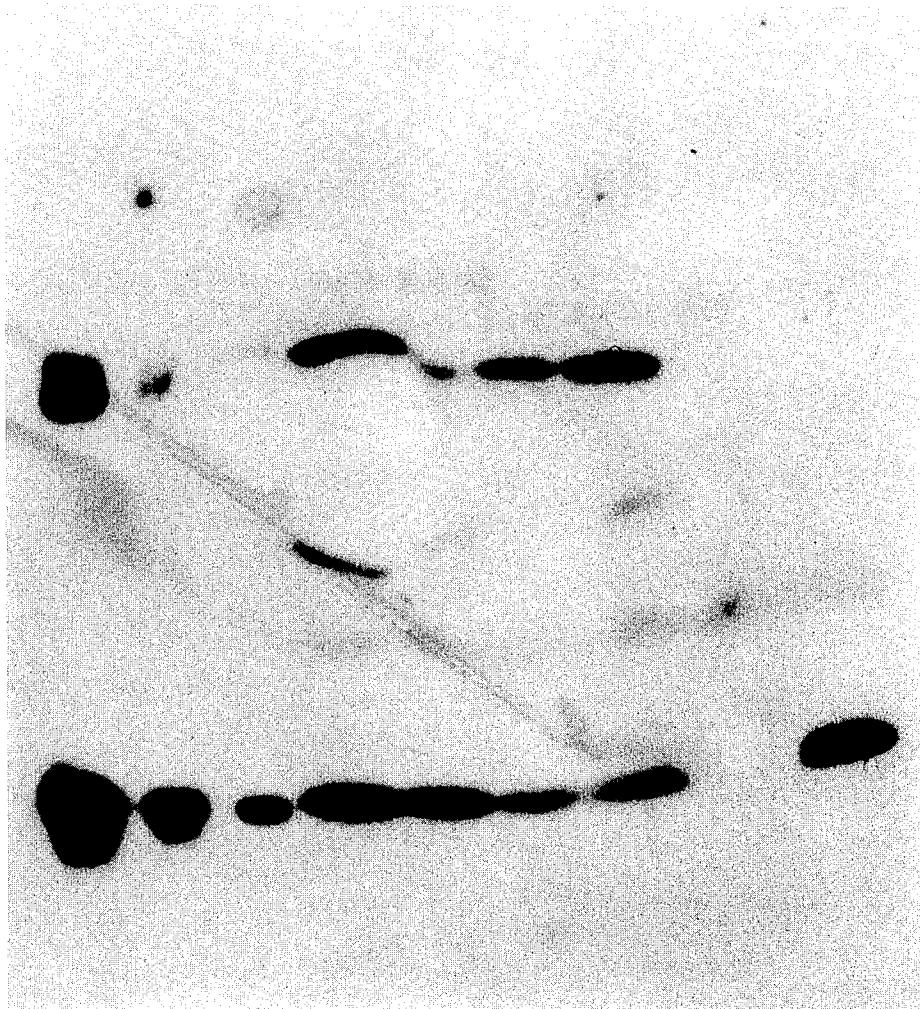


Fig. 8A.





1 2 3 4 5 6 7 8 9

Fig. 8C.

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