United States Patent [19] 4,816,397 Patent Number: Date of Patent: Boss et al. Mar. 28, 1989 [54] MULTICHAIN POLYPEPTIDES OR 041313 12/1981 European Pat. Off. . 041767 12/1981 European Pat. Off. . PROTEINS AND PROCESSES FOR THEIR 055945 7/1982 European Pat. Off. . PRODUCTION 075444 3/1983 European Pat. Off. . European Pat. Off. [75] Inventors: Michael A. Boss, Slough; John H. 088994 9/1983 Kenten; John S. Emtage, both of 0125023 11/1984 European Pat. Off. High Wycombe; Clive R. Wood, OTHER PUBLICATIONS Near Fordingbridge, all of United Adams et al., Biochemistry, vol. 19, pp. 2711-2719, Kingdom Celltech, Limited, Slough, United [73] Assignee: Haley et al., DNA, vol. 1, pp. 155-162, 1982. Kingdom Gough et al., Biochemistry, vol. 19, pp. 2702-2710, 672,265 [21] Appl. No.: Iserentant et al., Gene, vol. 9, pp. 1-12, 1980. [22] PCT Filed: Mar. 23, 1984 Seidman et al: "Immunoglobulin light-chain structural [86] PCT No.: PCT/GB84/00094 gene sequences cloned in a bacterial plasmid," Nature, vol. 271, pp. 582-585, 1978. § 371 Date: Nov. 14, 1984 Primary Examiner-Blondel Hazel § 102(e) Date: Nov. 14, 1984 Attorney, Agent, or Firm-Cushman, Darby & Cushman [87] PCT Pub. No.: WO84/03712 ABSTRACT PCT Pub. Date: Sep. 27, 1984 Multichain polypeptides or proteins and processes for their production in cells of host organisms which have [30] Foreign Application Priority Data been transformed by recombinant DNA techniques. Mar. 25, 1983 [GB] United Kingdom 8308235 According to a first aspect of the present invention, [51] Int. Cl.4 C12P 21/00; C12N 15/00; there is provided a process for producing a heterolo-C12N 1/00; C12N 1/20 gous multichain polypeptide or protein in a single host [52] U.S. Cl. 435/68; 435/172.3; cell, which comprises transforming the host cell with 435/243; 435/255; 435/320; 435/252.31; DNA sequences coding for each of the polypeptide 435/252.33 chains and expressing said polypeptide chains in said transformed host cell. According to another aspect of [58] Field of Search 435/68, 172.3, 243, 435/320, 253, 255 the present invention there is provided as a product of recombinant DNA technology an Ig heavy or light References Cited [56] chain or fragment thereof having an intact variable U.S. PATENT DOCUMENTS domain. The invention also provides a process for increasing the level of protein expression in a transformed 4,403,036 9/1983 Hartley et al. 435/68 host cell and vectors and transformed host cells for use 4,642,334 2/1987 Moore et al. 435/68 in the processes. FOREIGN PATENT DOCUMENTS

037723 10/1981 European Pat. Off. .

18 Claims, 13 Drawing Sheets



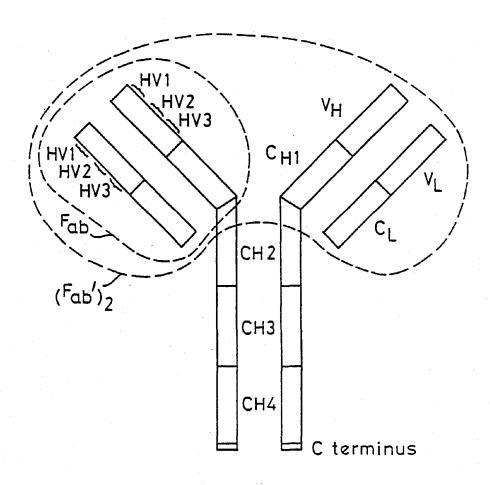
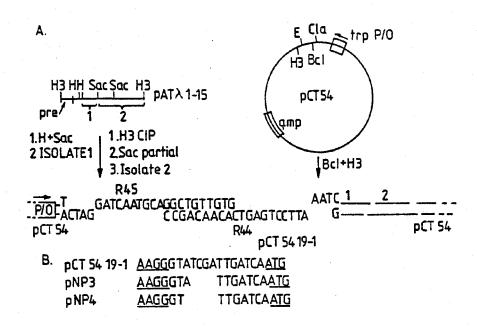


FIG. 1



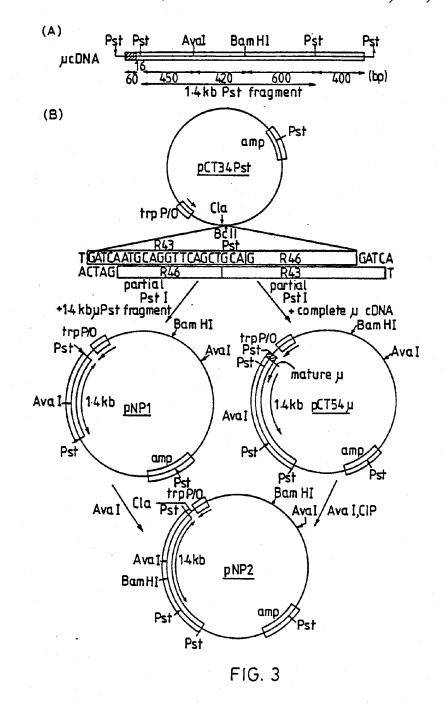
Legend. E = E corRI

H = HinfI

H3= Hind III

FIG. 2





Possible 2° structures of µ mRNAs

5'→3'

pNP9.

G G G A G = 7.6 K.cal.

A=U (1.0 ru)

C=G

G=C
A=GGGUAUGAUCAAU=AGCAGC
AGGGUAUGAUCAAU=AGCAGC
AGGGUAUGAUCAGCAGCAGC
AGGGUAUGAUCAGCAGCAGC
AGGGUAUGAGCAGCAGC
AAGGGUAU=ACUGCAGCAGCAGC-

U C U A G G ΔG=7.6 K cal G=C (1.8 ru) C=G G=C - AAGGUAUUGCACAUAU=AGCAGC-

pNP14. (101-2 ru)

-<u>AAGG</u>GUAUGAUCA<u>AUG</u>CAAGUGCAACUGCAG

FIG. 4

DOCKET

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