## United States Patent [19]

#### Boss et al.

#### [54] MULTICHAIN POLYPEPTIDES OR PROTEINS AND PROCESSES FOR THEIR PRODUCTION

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- [73] Assignee: Celltech, Limited, Slough, United Kingdom
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- § 102(e) Date: Nov. 14, 1984
- [87] PCT Pub. No.: WO84/03712
- PCT Pub. Date: Sep. 27, 1984
- [30] Foreign Application Priority Data
- Mar. 25, 1983 [GB] United Kingdom ...... 8308235
- [51] Int. Cl.<sup>4</sup> ..... Cl2P 21/00; Cl2N 15/00;
- 435/243; 435/255; 435/320; 435/252.331; 435/252.33

#### [56] References Cited

#### **U.S. PATENT DOCUMENTS**

4,403,036	9/1983	Hartley et al 435/68	
4,642,334	2/1987	Moore et al 435/68	

#### FOREIGN PATENT DOCUMENTS

037723 10/1981 European Pat. Off. .

## [11] Patent Number: 4,816,397

#### [45] Date of Patent: Mar. 28, 1989

041313 12/1981	European Pat. Off
041767 12/1981	European Pat. Off
055945 7/1982	European Pat. Off
075444 3/1983	European Pat. Off
088994 9/1983	European Pat. Off
0125023 11/1984	European Pat. Off

#### OTHER PUBLICATIONS

Adams et al., Biochemistry, vol. 19, pp. 2711-2719, 1980.

Haley et al., DNA, vol. 1, pp. 155-162, 1982.

Gough et al., Biochemistry, vol. 19, pp. 2702-2710, 1980.

Iserentant et al., Gene, vol. 9, pp. 1-12, 1980.

Seidman et al: "Immunoglobulin light-chain structural gene sequences cloned in a bacterial plasmid," *Nature, vol. 271, pp. 582-585, 1978.* 

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#### [57] ABSTRACT

Multichain polypeptides or proteins and processes for their production in cells of host organisms which have been transformed by recombinant DNA techniques. According to a first aspect of the present invention, there is provided a process for producing a heterologous multichain polypeptide or protein in a single host cell, which comprises transforming the host cell with DNA sequences coding for each of the polypeptide chains and expressing said polypeptide chains in said transformed host cell. According to another aspect of the present invention there is provided as a product of recombinant DNA technology an Ig heavy or light chain or fragment thereof having an intact variable domain. The invention also provides a process for increasing the level of protein expression in a transformed host cell and vectors and transformed host cells for use in the processes.

#### 18 Claims, 13 Drawing Sheets

Sanofi/Regeneron Ex. 1012, pg 407

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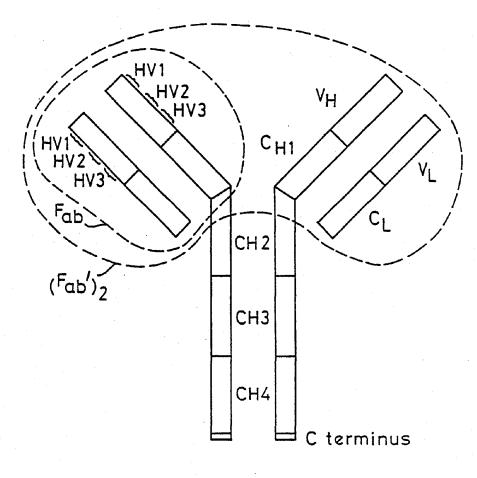
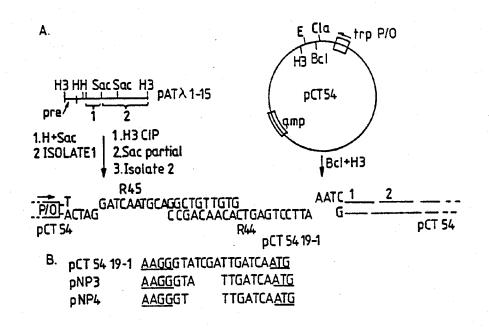


FIG. 1

Sanofi/Regeneron Ex. 1012, pg 408

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Legend. E = E corRI H = HinfI H3= Hind III

FIG. 2

Sanofi/Regeneron Ex. 1012, pg 409

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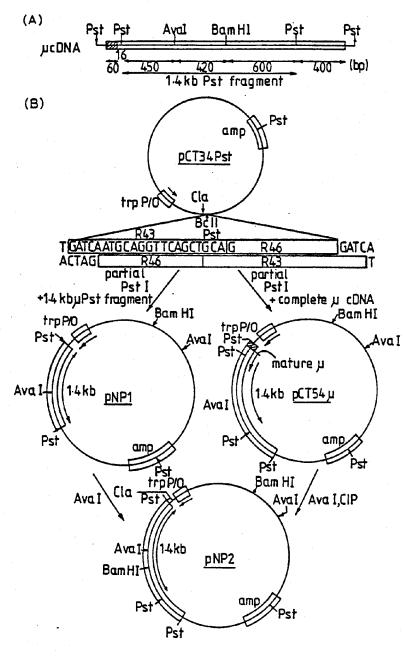


FIG. 3

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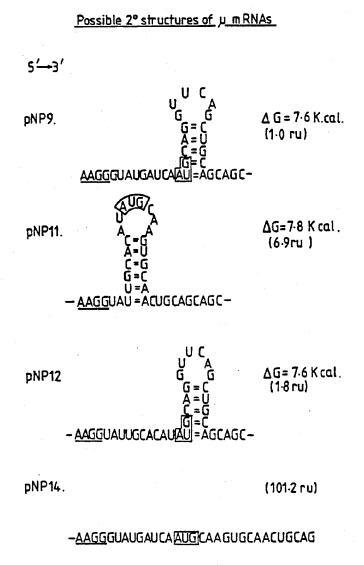


FIG. 4

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