(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 July 2004 (22.07.2004)

PCT

(10) International Publication Number
WO 2004/061104 A3

(51) International Patent Classification[7]: C12N 15/10, 5/10, 15/85, 15/64, C07K 16/00, 14/705, A61K 39/395, 38/17

(21) International Application Number: PCT/DK2004/000001

(22) International Filing Date: 7 January 2004 (07.01.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

PA 2003 00008	7 January 2003 (07.01.2003)	DK
60/438,403	7 January 2003 (07.01.2003)	US
60/476,018	5 June 2003 (05.06.2003)	US

(71) Applicant *(for all designated States except US)*: **SYMPHOGEN A/S** [DK/DK]; Elektrovej, Bygning 375, DK-2800 Kongens Lyngby (DK).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **HAURUM, John, S.** [DK/DK]; Gustav Adolfsgade 6, 3.th., DK-2100 København Ø (DK). **WIBERG, Finn, C.** [DK/DK]; Vinkelvej 16, DK-3520 Farum (DK). **COLJEE, Vincent, W.** [NL/DK]; Brovænget 19, DK-2830 Virum (DK). **SHARON, Jacqueline** [US/US]; 478 Clinton Road, Chestnut Hill, MA 02467 (US). **YANG, Chiou-Ying**; 336 Ho Tso St. 5F, 402 Taichung (TW) (TW).

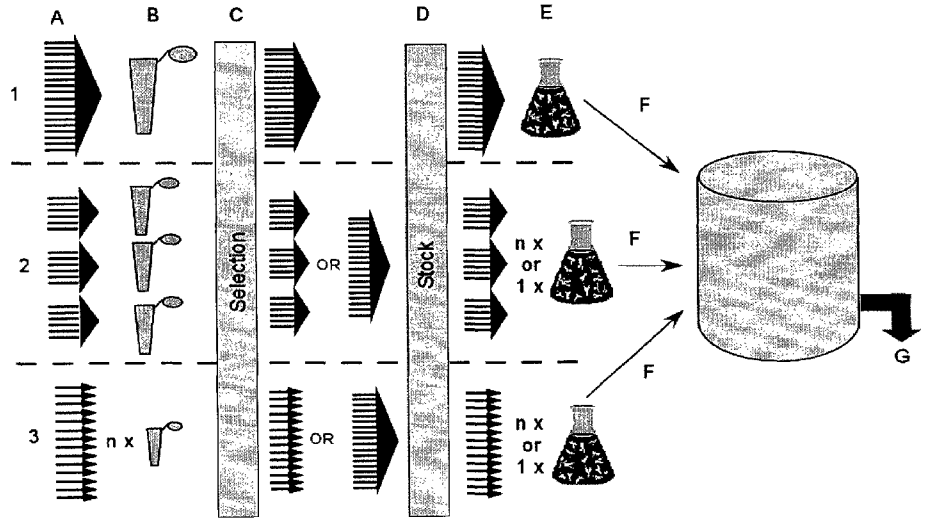
(74) Agent: **INSPICOS A/S**; P.O. Box 45, Bøge Allé 3, DK-2970 Hørsholm (DK).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,

[Continued on next page]

(54) Title: METHOD FOR MANUFACTURING RECOMBINANT POLYCLONAL PROTEINS



(57) Abstract: The invention relates to a method for manufacturing a recombinant polyclonal protein composition, in particular a recombinant polyclonal antibody composition. The method comprises obtaining a collection of cells transfected with a library of variant nucleic acid sequences, wherein each cell in the collection is transfected with and capable of expressing one member of the library, which encodes a distinct member of a polyclonal protein that binds a particular antigen and which is located at the same single site in the genome of individual cells in said collection, wherein said nucleic acid sequence is not naturally associated with said cell in the collection. The cells are cultured under suitable conditions for expression of the polyclonal protein, which is obtained from the cells or culture supernatant. The nucleic acid sequence id introduced into the cells by transfection with a library of vectors for site-specific integration. The present method is suitable for manufacturing recombinant polyclonal antibodies, thereby making available a superior replacement of plasma-derived therapeutic immunoglobulin products.

WO 2004/061104 A3

GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
4 November 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.