

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
23 June 2005 (23.06.2005)

PCT

(10) International Publication Number
WO 2005/055957 A2

- (51) International Patent Classification⁷: **A61K**
- (21) International Application Number: PCT/US2004/041879
- (22) International Filing Date: 9 December 2004 (09.12.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
 - 10/732,862 10 December 2003 (10.12.2003) US
 - 10/787,734 26 February 2004 (26.02.2004) US
- (71) Applicants: **APOVIA, INC.** [US/US]; 11125 Flintkote, Suite A, San Diego, CA 92121 (US). **VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECHNOLOGIE** [BE/BE]; Rijvisschestraat 118, Bus 1, B-9052 Zwijnaarde (BE).
- (72) Inventors: **BIRKETT, Ashley**; 2409 Okd Ranch Road, Escondido, CA 92027 (US). **FIERS, Walter**; Beukendreef 3, B-9070 Destelbergen (BE).
- (74) Agents: **GAMSON, Edward, P.** et al.; Welsh & Katz, Ltd., 120 South Riverside Plaza, 22nd Floor, Chicago, IL 60606 (US).
- (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, 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, 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, NA, SD, SL, SZ, TZ, UG, ZM,

[Continued on next page]

(54) Title: INFLUENZA IMMUNOGEN AND VACCINE

A

Ground Squirrel wylfhlclvf acvpcptvqa sklclglwld

1

HBc AYW mdidykcfg atvellsfpl sdiffpsvrdl ldtasalyre
 HBc ADW mdidykefg atvellsfpl sdiffpsvrdl ldtasalyre
 HBc ADW2 mdidykefg atvellsfpl sdiffpsvrdl ldtasalyre
 HBc ADYW mdidykefg atvellsfpl sdiffpsvrdl ldtasalyre
 Woodchuck mdidykefg ssyqlnflpl ldfppdlnal vdtatalyee
 Ground Squirrel mdidykefg ssyqlnflpl ldfppdlnal vdtatalyee

41

HBc AYW alespehcsp hhtairgail cwgelmtlat wvgvnlqdp
 HBc ADW alespehcsp hhtairgail cwgelmtlat wvgvnlqdp
 HBc ADW2 alespehcsp hhtairgail cwgelmtlat wvgvnlqdp
 HBc ADYW alespehcsp hhtairgail cwgelmtlat wvgvnlqdp
 Woodchuck eltgrehcsp hhtairgalv cweeltrlit wmsentteeq
 Ground Squirrel eltgrehcsp hhtairgalv cweeltrlit wmsentteeq

B

81

HBc AYW srdlvvsyvn tmnglkfrql lwfhiscitf gretvleylv
 HBc ADW srdlvvsyvn tmnglkfrql lwfhiscitf gretvleylv
 HBc ADW2 srdlvvsyvn tmnglkfrql lwfhiscitf gretvleylv
 HBc ADYW srdlvvsyvn tmnglkfrql lwfhiscitf gretvleylv
 Woodchuck vrriivnhvn dtwglkvrqs lwfhiscitf gqhtvqeflv
 Ground Squirrel rriivdhvnn twglkvrqtl wfhiscitfg qhtvqeflvs

121

HBc AYW sfgvwirtpp ayrppnapil stlpettvvr rrgsrprrr
 HBc ADW sfgvwirtpp ayrppnapil stlpettvvr rrdgrsprrr
 HBc ADW2 sfgvwirtpp ayrppnapil stlpettvvr rrdgrsprrr
 HBc ADYW sfgvwirtpp ayrppnapil stlpettvvr rrgsrprrr
 Woodchuck sfgvwirtppa pyrppnapil stlpettvir rrgsraars
 Ground Squirrel fgvwirtppa yrppnapils tlpettvirr rrgsraars

161

HBc AYW psprrrrsqs prrrrsqsere sqc
 HBc ADW rtpsprrrrs qsprrrrsqs rcsqc
 HBc ADW2 rtpsprrrrs qsprrrrsqs resqc
 HBc ADYW psprrrrsqs prrrrsqsere sqc
 Woodchuck prrrrpsprrr rrsqsprrrr sqc
 Ground Squirrel rritpsprrr rrsqsprrrrs qspasnc

(57) Abstract: A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid (HBc) protein is disclosed that contains an immunogen for inducing the production of antibodies to the influenza M2 protein. An immunogenic influenza sequence in two to four copies is preferably expressed at or near the N-terminus or in the HBc immunogenic loop sequence. The HBc chimera preferably contains an influenza-specific T cell epitope and is preferably engineered for both enhanced stability of self-assembled particles and enhanced yield of those chimeric particles. Methods of making and using the chimeras are also disclosed.

WO 2005/055957 A2