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(54) **MONOCLONAL ANTIBODIES AND
COMPLEMENTARITY-DETERMINING
REGIONS BINDING TO EBOLA
GLYCOPROTEIN**

(75) Inventors: **Mary Kate Hart**, Frederick, MD (US);
Julie Wilson, Birmingham, AL (US)

(73) Assignee: **The United States of America as
represented by the Secretary of the
Army**, Washington, DC (US)

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530/300; 435/345**

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435/91.1, 69.1, 345; 530/300

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,792,462	A	8/1998	Johnston et al.	424/199.1
5,977,316	A *	11/1999	Chatterjee et al.	530/387.2
6,340,463	B1	1/2002	Mitchell et al.	424/263.1
6,630,144	B1 *	10/2003	Hart et al.	424/159.1
2003/0224015	A1	12/2003	Hart et al.		
2004/0146859	A1	7/2004	Hart et al.		

FOREIGN PATENT DOCUMENTS

WO	WO 96/37616	11/1996
WO	WO 99/32147	7/1999
WO	WO 00/00617	A2 1/2000
WO	WO 01/016183	A1 * 3/2001

OTHER PUBLICATIONS

Maruyama et al, Journal of Virology, Jul. 1999, vol. 73, No. 7, pp. 6024–6030.*

Wilson et al., “Vaccine Potential of Ebola Virus VP24, VP30, VP35 and VP40 Proteins”, Virology 286, pp. 384–390 (2001).

Wilson and Hart, “Protection from Ebola Virus Mediated by Cytotoxic T Lymphocytes Specific for the Viral Nucleoprotein”, Journal of Virology, Mar. 2001, vol. 75, No. 6, pp. 2660–2664.

Pushko et al., “Venezuelan Equine Encephalitis Virus Replicon Vector: Immunogenicity Studies with Ebola NP and GP Genes in Guinea Pigs”, Vaccines 97, Molecular Approaches to the Control of Infectious Diseases, Cold Spring Harbor Laboratory Press, 1997, pp. 253–258.

Geisbert et al., “Evaluation in Nonhuman Primates of Vaccines Against Ebola Virus”, Emerging Infectious Diseases, vol. 8, No. 5, May 2000, pp. 503–507.

Pushko et al., “Recombinant RNA Replicons Derived from Attenuated Venezuelan Equine Encephalitis Virus Protect Guinea Pigs and Mice from Ebola Hemorrhagic Fever Virus”, JVAC, Vaccine, pp. 1–12.

Abstract, W33–5, Hooper et al., “DNA Vaccination Against Poxviruses Using Combinations of IMV and EEV Immunogens”, Jul. 2000, American Society for Virology Meeting.

Abstract, P23–6, Hooper et al., DNA Immunization with the Vaccinia L1R and/or A33R genes, Jul. 1998, Poster at American Society for Virology Meeting.

Meyer et al., “Identification of Binding Sites for Neutralizing Monoclonal Antibodies on the 14–kDa Fusion protein of Orthopox Viruses”, Virology 200, pp. 778–783 (1994).

Czerny and Mahnel, “Structural and functional analysis of orthopoxvirus epitopes with neutralizing monoclonal antibodies”, J. General Virology (1990), vol. 71, pp. 2341–2352.

Hooper et al., “DNA Vaccination with Vaccinia Virus L1R and A33R Genes Protects Mice Against a Lethal Poxvirus Challenge”, Virology 266, pp. 329–339 (2000).

Vazquez and Esteban, “Identification of Functional Domains in the 14–Kilodalton Envelope Protein (A27L) of Vaccinia Virus”, J. Virology, vol. 73, No. 11, Nov. 1999, pp. 9098–9109.

Vazquez et al., “The Vaccinia Virus 14–Kilodalton (A27L) Fusion Protein Forms a Triple Coiled–Coil Structure and Interacts with the 21–Kilodalton (A17L) Virus Membrane Protein through a C–Terminal alpha–Helix”, J. Virology, vol. 72, No. 12, Dec. 1998, pp. 10126–10137.

Rodriguez et al., “The Vaccinia Virus 14–Kilodalton Fusion Protein Forms a Stable Complex with the Processed Protein Encoded by the Vaccinia Virus A17L Gene”, J. Virology, vol. 67, No. 6, Jun. 1993, pp. 3435–3440.

Lai et al., “The Purified 14–Kilodalton Envelope Protein of Vaccinia Virus Produced in *Escherichia coli* Induces Virus Immunity in Animals”, J. Virology, vol. 65, No. 10, Oct. 1991, pp. 5631–5635.

Rodriguez and Esteban, “Mapping and Nucleotide Sequence of the Vaccinia Virus Gene That Encodes a 14–Kilodalton Fusion Proteins”, J. Virology, Nov. 1987, vol. 61, No. 11, pp. 3550–3554.

Rodriguez et al., “Isolation and Characterization of Neutralizing Monoclonal Antibodies to Vaccinia Virus”, J. Virology, Nov. 1985, vol. 56, No. 2, pp. 482–488.

(Continued)

Primary Examiner—Ali R. Salimi
(74) *Attorney, Agent, or Firm*—Elizabeth Arwine

(57) **ABSTRACT**

In this application are described Ebola GP monoclonal antibodies, epitopes recognized by these monoclonal antibodies, and the sequences of the variable regions of some of these antibodies. Also provided are mixtures of antibodies of the present invention, as well as methods of using individual antibodies or mixtures thereof for the detection, prevention, and/or therapeutical treatment of Ebola virus infections in vitro and in vivo.

6 Claims, 2 Drawing Sheets