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(54) **METHODS FOR PRODUCING MARBURG VIRUS PROTEINS**

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(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,792,462	A *	8/1998	Johnston et al.	424/199.1
5,811,407	A *	9/1998	Johnston et al.	514/44
6,541,010	B1 *	4/2003	Johnston et al.	424/199.1

OTHER PUBLICATIONS

Hevey et al (Virology 239:206-216, 1997).*

Becker et al (Virology 225:145-155, 1996).*

Pushko et al (Virology 239:389-401, 1997).*

Pushko et al (Vaccines 97, p. 253-258, 1997).*

Vanderzanden et al., "DNA Vaccines Expressing Either the GP or NP Genes of Ebola Virus Ptoect Mice from Lethal Challenge", Virology 245, 000-000 (1998), pp. 1-10.

Xu et al., "Immunization for Ebola Virus infection", Nature Medicine, vol. 4, No. 1, Jan. 1998, pp. 37-42.

Bray et al., "A mouse model for evaluatio n of prophylaxis and therapy of Ebola hemorrhagive fever", J. Infectious Diseases, 1998, 178:651-61.

Will et al., "Marburg virus gene 4 enclosed the virion membrane protein, a Type I transmembrane glycoprotein", J. Virology, Mar. 1993, vol. 67, No. 3, p. 1203-1210.

Sanchez et al., "Sequence analysis of the Marburg virus nucleoprotein gene: comparison to Ebola virus and other non-segmented negative-strand RNA viruses", J. Gen. Virology (1992) 73:347-357.

Feldmann et al., "Glycosylation and oligomerization of the spike protein of Marburg virus", Virology 182, 353-356 (1991).

Feldmann et al., "Characterization of Filoviruses based on differences in structure and antigenicity of the virion glycoprotein", Virology 199, 469-473 (1994).

Johnson et al., "Lethal experimental infections of rhesus monkeys by aerosolized Ebola virus", Int. J. Exp. Path. (1995) 76:227-236.

Volchkov et al., "Processing of the Ebola virus glycoprotein by the proprotein convertase furin", PNAS USA, vol. 95, pp. 5762-5767 (May 1998).

Smith et al., "Fatal Human Disease from Vervet Monkeys", Preliminary Communications, The Lancet, No. 7256, Nov. 25, 1967, pp. 1119 and 1121.

Lupton et al., "New Activated Factor IX Product in Haemophilia", Letters to the Editor, The Lancet, Dec. 13, 1980, pp. 1294-1295.

Ignat'ev et al., "Comparative analysis of some immunological parameters of inactivated Marbug virus injected into guinea pigs", Voprosy Virusologii, No. 5, pp. 118-120, 1991.

Hevey et al., "Antigenicity and vaccine potential of Marburg virus glycoprotein expressed by Baculovirus recombinants", Virology 239:206-216 (1997).

Hevey et al., "Recombinant Marburg Virus glycoprotein subunit vaccine protects guinea pigs from lethal infection", Vaccines 97, 1997, pp. 93-98.

Connolly et al, "Pathogenesis of experimental Ebola virus infection in guinea pigs", J. Infectious Diseases, 1999: 179(suppl 1): S203-17.

Ignatyev et al, "Inactivated Marburg virus elicits a nonprotective immune response in Rhesus monkeys", J. Biotechnology 44 (1996) 111-118.

Caley et al, "Humoral, mucosal, and cellular immunity in response to a human immunodeficiency virus Type I immunogen expressed by a Venezuelan Equine Encephalitis virus vaccine vector", J. Virology, Apr. 1997, vol. 71, No. 4, p. 3031-3038.

Kiley et al, "Filoviridae: a taxonomic home of Marburg and Ebola Viruses?", Taxonomy, Intervirology 18:24-32, (1982).

Feldmann et al., "Marburg virus, a filovirus: messenger RNAs, gene order, and regulatory elements of the replication cycle", Virus Research, 24 (1992) 1-19.

Pushko et al., "Replicon-helper systems from attenuated Venezuelan Equine Encephalitis virus: expression of heterologous genes in vitro and immunization against heterologous pathogens in vivo", Virology 239:389-401 (1997).

(Continued)

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(57) **ABSTRACT**

Using the MBGV GP, NP, and virion proteins, a method and composition for use in inducing an immune response which is protective against infection with MBGV in nonhuman primates is described.