The Development of Prophylactic EBV Vaccines

Man Wang* and Shuai Jiang

1Institute for Translational Medicine, Medical College of Qingdao University, Qingdao, 266021, P.R. China
2State Key Laboratory of Virology, College of Life Sciences, Wuhan University, Wuhan, 430072, P.R. China

Epstein-Barr virus (EBV) is an important global human pathogen found in over 90% of the world's population [1]. EBV infection usually occurs in young children and causes no or only nonspecific symptoms [2]. However, EBV is the major cause of infectious mononucleosis (IM) [3]. EBV is an oncogenic virus associated with various human malignancies of both epithelial and lymphoid origin such as nasopharyngeal carcinoma (NPC), a subset of gastric carcinoma (GC), Burkitt's lymphoma (BL), Hodgkin lymphoma (HL) and post-transplant lymphoproliferative disorder (PTLD) [4,5]. Almost 200,000 cases of EBV-associated malignancies occur each year worldwide [6]. Currently, no vaccine has been licensed to prevent EBV infection or EBV-associated diseases. There is an urgent need for the development of EBV vaccines. Although a vaccine to prevent EBV infection was proposed as long ago as 1973 [7], the development of an EBV vaccine has been agonizingly slow.

EBV major envelope glycoprotein gp350 has been widely considered as an attractive candidate for a prophylactic EBV vaccine. The reason for choosing gp350 is that EBV causes infection predominantly by binding gp350 to the CD21 receptor on the surface of B lymphocytes [8]. Numerous studies have demonstrated the efficacy of gp350-based vaccines [9-11]. Prophylactic EBV vaccines have been evaluated in controlled clinical trials [12] vaccinated adults, children and infants in China with a single dose of vaccinia virus expressing gp350. The gp350 vaccination was able to elicit neutralizing antibodies in the 9 EBV-seronegative children (100%), and only 3 of the 9 vaccinated children were infected with EBV during 16 months of follow-up. The vaccine could not effectively elicit EBV antibodies in EBV-seropositive and vaccinia virus-seropositive adults, hinting that this gp350 vaccine might be recommended for EBV-seronegative children. However, vaccinia virus is unlikely to be accepted as a vaccine vector because of its potential side effects.

In a phase I/II study, recombinant gp350 expressed in Chinese hamster ovary (CHO) cells exhibited the ability to induce neutralizing antibodies in healthy volunteers [13]. The subjects receiving soluble gp350 in no adjuvant developed lower levels of EBV antibodies than those receiving soluble gp350 in alum/monophosphoryl lipid A. These results demonstrated that the adjuvant could enhance the humoral immunity in vaccine recipients. A phase II, randomized, double-blind placebo-controlled trial of soluble gp350 was performed in 181 EBV-seronegative children [14], the gp350 vaccine could elicit EBV neutralizing antibodies and reduce the rate of IM, but failed to prevent EBV infection. The gp350 vaccine is more effective than gp350 alone. The vaccine efficacy of a mixture of EBV antigens should be evaluated in future clinical trials. For example, other EBV antigens such as EBNA3A [19] and LMPs [20] could induce antigen-specific T-cell responses and were promising vaccine candidates against EBV-associated malignancies. Furthermore, to avoid possible side effects caused by EBV vaccines, the optimum vaccine formulation, including both the antigen and adjuvant, needs to be determined in the following trials.

Acknowledgements

This work was supported by the Promotive Research Fund for Excellent Young and Middle-Aged Scientists of Shandong Province (No. BS2014YY042).

References


*Corresponding author: Man Wang, Institute for Translational Medicine, Medical College of Qingdao University, Qingdao, 266021, China, Tel: +86-532-82991791; E-mail: wangman@qdu.edu.cn

Received: October 26, 2015; Accepted: October 29, 2015; Published: November 02, 2015


Copyright: © 2015 Wang M, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.


