A LYMPH NODE TARGETED MOLECULAR ADJUVANT AND ENGINEERED SUBUNIT ANTIGEN VACCINE PROMOTES POTENT CELLULAR AND HUMORAL IMMUNITY TO EPSTEIN-BARR VIRUS IN HLA-EXPRESSING MICE

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Abstract

Epstein-Barr virus (EBV) is a gamma-herpesvirus which infects over 95% of people worldwide. EBV is associated with infectious mononucleosis, numerous malignancies of B cell and epithelial origin and the development of autoimmune disorders, particularly multiple sclerosis. Here we describe a novel subunit vaccine formulation based on a lymph node targeting amphiphile (AMP) vaccine adjuvant, AMP-CpG, composed of diacyl lipid-modified CpG DNA, admixed with EBV gp350 glycoprotein and an EBV-polyepitope protein (EBVpoly) that includes 20 $CD8^+$ T cell epitopes from EBV latent and lytic antigens. Potent gp350-specific IgG responses were induced in HLA-expressing mice as early as 3 weeks after the first dose with titers >100,000 by one week post second dose in AMP-CpG vaccinated mice. In addition, sera from AMP-CpG immunized mice exhibited approximately 100-fold increased neutralizing antibody titers compared to soluble CpG vaccinated mice. Immunization including AMP-CpG also induced high frequencies of polyfunctional ($IFN\gamma^+$ $TNF\alpha^+$ $IL2^+$) gp350-specific $CD4^+$ T cells and EBVpoly-specific $CD8^+$ T cells that were 2-fold greater than soluble CpG comparators. More importantly, these EBV-specific T-cell and antibody responses were maintained for >7 months post immunization, suggesting the potential for durable immune protection. The broad coverage induced against multiple viral determinants facilitated by the enhanced lymph node delivery of AMP-CpG adjuvant is likely to provide better protection against primary infection while the strong T cell responses will be critical to control the spread of latently infected B cells and the development of EBV-associated diseases.