antiviral response and is a novel aspect of its mechanism of action.

doi:10.1016/j.antiviral.2007.01.043

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Vaccination as an Antiviral Strategy for Control of Cytomegalovirus (CMV) Disease: A Vectored Vaccine Approach Targeting the UL83 (pp65) Homolog Protects Against Congenital CMV Disease in the Guinea Pig Model

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Development of vaccines against cytomegalovirus (CMV) infection is a major priority, both for high-risk immunosuppressed patients, and to protect against disabling congenital infections. Glycoprotein subunit vaccines have demonstrated efficacy against disease in small animal models of congenital CMV infection, but to date there have been no reports of the use of vaccines targeting tegument proteins such as pp65 (UL83), the major target of anti-CMV cytotoxic T-lymphocyte responses, in this setting. We report the use of a propagation-defective, single cycle, RNA replicon vector system, derived from an attenuated strain of the alphavirus Venezuelan equine encephalitis (VEE) virus, to produce virus-like replicon particles (VRP) expressing GP83, the guinea pig CMV (GPCMV) homolog of the human CMV pp65 phosphoprotein encoded by the UL83 gene. Vaccination with VRP GP83 induced antibodies and CD4+ and CD8+ T cell responses in GPCMV-seronegative female guinea pigs. Guinea pigs immunized with VRP-GP83 vaccine, or a VRP vaccine expressing influenza hemagglutinin (VRP-HA), were bred for pregnancy and subsequent GPCMV challenge. After early third trimester challenge with GPCMV, dams previously vaccinated with VRP-GP83 had improved pregnancy outcomes compared to dams previously vaccinated with the VRP-HA control. Among VRP-GP83-vaccinated dams, there were 28 live pups, and 4 dead pups (13% mortality) among 10 evaluable litters, compared to 9 live pups and 12 dead pups (57% mortality) among 8 evaluable litters in the VRP HA vaccinated group ($p < 0.001$, Fisher's exact test). The improved pregnancy outcome was accompanied by reduction in maternal whole blood viral load as measured by real-time PCR. These results indicate that cell-mediated immune responses directed against a CMV matrix protein can protect against congenital CMV infection.

doi:10.1016/j.antiviral.2007.01.044

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JuvImmune is a Novel Vaccine Adjuvant that Enhances Protection of Mice from Lethal HSV-2 Infection Following Immunization

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Genital herpes simplex type 2 (HSV-2) infection is common and an effective vaccine remains a priority. We therefore examined the efficacy of JuvImmune as a vaccine adjuvant against genital HSV-2 infection in mice. JuvImmune, a complex of lipid carrier and non-coding DNA, enhances protection against several viral and bacterial diseases. In our studies, out-bred Swiss Webster mice (12 animals/group) were immunized IP twice at 3-week intervals with a detergent-inactivated whole HSV-2 vaccine or controls. Groups included placebo, vaccine (VAC) alone, JuvImmune alone, JuvImmune + VAC or MPL + VAC. Three weeks post boost, mice were treated with progesterone and given a lethal intravaginal challenge of HSV-2 (5×10^5 pfu). Vaginal swabs were collected on days 1–4 post challenge and serum was collected at 3 and 5 weeks post immunization. Our preliminary results indicate that animals immunized with JuvImmune + VAC developed higher antibody titers compared to VAC alone or MPL + VAC after the first immunization. Mice were followed for 21 or 30 days in two separate experiments. The JuvImmune + VAC immunization reduced HSV-2 disease symptoms compared to MPL + VAC. In the first experiment, JuvImmune + VAC completely protected mice from death at 21 days compared to a mortality of 40% in the MPL + VAC group ($P < 0.037$). In the second experiment, JuvImmune + VAC protected 83% of the mice from death at day 21, and 75% of mice at 30 days post challenge, compared to only 17% at both 21 days ($P < 0.003$) and 30 days ($P > 0.036$) in the MPL + VAC group. In both experiments, vaginal titers were also reduced at day 2 in the JuvImmune + VAC group compared to all other groups. These results suggest that the JuvImmune adjuvant is superior to the MPL adjuvant in protecting mice from genital HSV-2 infection. Further studies are planned to determine the mechanisms of protection provided by the JuvImmune adjuvant.

Acknowledgement: Supported by Contract NO1-AI-15438 from the Virology Branch, NIAID, NIH.

doi:10.1016/j.antiviral.2007.01.045