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ROTAVIRUS VP6 NANOTUBES SHOW AN ANTIGEN FORM-DEPENDENT ADJUVANT ACTIVITY: ZIKA VIRUS ENVELOPE PROTEIN MONOMER VS ZIKA VIRUS-LIKE PARTICLES

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The structural protein of rotavirus (RV) VP6 can self-assemble into tubular polymeric structures under specific conditions of pH and ionic strength when expressed in recombinant systems. Previous studies have shown that RV VP6 nanotubes (VP6NT) have an adjuvant effect on the immunogenicity of norovirus virus-like particles (VLPs) in mice (Blazevic et al., 2011; Malm et al., 2016). The present study focused on the determination of adjuvant activity of VP6NT on the immunogenicity of monomers of the viral envelope (E) protein or of Zika virus (ZikV) VLPs. ZikV infection can cause congenital malformations in fetuses and the Guillain-Barré syndrome in adults, as the most severe consequences. To date, there is no treatment or vaccine available against ZikV. Several vaccine candidates against this virus have been reported and E protein has been selected as the primary antigenic determinant.

To evaluate the adjuvant properties of VP6NT on the E protein monomer or on ZikV VLPs, groups of BALB/c mice were intramuscularly immunized with 0.5 µg or 10 µg of E protein alone or in combination with 5 or 10 µg of VP6NT or 5 µg of VLPs alone or in combination with 15 µg of VP6NT or phosphate buffer solution as a control. Blood samples were taken for the determination of anti-E protein, anti-VLPs, and anti-VP6NT antibodies by ELISA. Adjuvant activity of VP6NT on the immunogenicity of the E protein was not observed, as mice immunized with only E protein had higher or similar antibody titers than mice with co-administered VP6NT. A positive effect of VP6NT on the production of IgG specific to the E protein was found when the amount of co-administered VP6NT was increased from 5 µg to 10 µg. In contrast, we observed an adjuvant effect of VP6NT on ZikV VLPs, as anti-ZikV VLPs titers were over 2 times higher in the group co-administered with VP6NT compared to mice immunized with ZikV VLPs alone. We also detected an increase of cross-reactive antibodies for dengue virus serotype 2 (DenV-2) in samples from mice co-immunized with ZikV VLPs and VP6NT.

This study constitutes the first report of the use of VP6NT as an adjuvant for a vaccine against ZikV. Here, we demonstrate that the adjuvant activity of VP6NT depends on whether the vaccine is formulated by a soluble antigen such as ZikV E protein monomer or by a particulate antigen such as ZikV VLPs. Although more studies are necessary to understand the effect of VP6NT on cellular and humoral immune responses, these results support the use of VP6NT as adjuvants and a great alternative when current commercial adjuvants are not desirable.

References

Blazevic, V., Lappalainen, S., Nurminen, K., Huhti, L., & Vesikari, T. (2011). Norovirus VLPs and rotavirus VP6 protein as combined vaccine for childhood gastroenteritis. Vaccine, 29(45), 8126-8133.

Malm, M., Tamminen, K., Lappalainen, S., Vesikari, T., & Blazevic, V. (2016). Rotavirus recombinant VP6 nanotubes act as an immunomodulator and delivery vehicle for norovirus virus-like particles. Journal of immunology research, 2016.