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Plant Expressed Vaccines Produce A Novel Synergistic Response Upon Co-delivery

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We have previously shown that plant-made recombinant immune complex (RIC) vaccines that consist of an antibody fused to a desired antigen and containing an antibody-specific epitope tag are a robust platform to improve the immunogenicity of weak antigens. In this study, we altered the antigen fusion site on the RIC platform to accommodate an N-terminal fusion to the IgG heavy chain (N-RIC) with a resulting 40% improvement in RIC expression over the normal C-terminal fusion (C-RIC). As a model antigen, the Zika envelope domain III (ZE3) protein was used. ZE3 has been identified as a safe and effective vaccine candidate, however, it is poorly immunogenic. Both types of RICs containing ZE3 were efficiently assembled in plants, purified to >95% homogeneity with a simple one-step purification, strongly bound complement receptor C1q, and elicited strong ZE3-specific antibody titers that correlated with ZIKV neutralization. When either N-RIC or C-RIC was co-delivered with hepatitis B core (HBc) virus-like particles (VLP) displaying ZE3, the combination elicited 5-fold greater antibody titers (>1,000,000) and more strongly neutralized ZIKV than either RICs or VLPs alone, after only two doses without adjuvant. These findings demonstrate that antigens that require a free N-terminus for optimal antigen display can be used with the RIC system and that plant-made RICs and VLPs are highly effective vaccines targeting ZE3. Thus, the RIC platform can be more generally applied to a wider variety of antigens to conveniently produce vaccine candidates against diseases.