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Extended Abstract

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

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Abstract

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.

Globally, researchers are undertaking significant efforts to design and develop effective vaccines, therapeutics, and antiviral drugs to curb the spread of coronavirus disease 2019 (COVID-19). Plants have been used for the production of vaccines, monoclonal antibodies, immunomodulatory proteins, drugs, and pharmaceuticals via molecular farming/transient expression system and are considered as bioreactors or factories for their bulk production. These biological products are stable, safe, effective, easily available, and affordable. Plant molecular farming could facilitate rapid production of biologics on an industrial scale, and has the potential to fulfill emergency demands, such as in the present situation of the COVID-19

pandemic. This article aims to describe the methodology and basics of plant biopharming, in addition to its prospective applications for developing effective vaccines and antibodies to counter COVID-19.

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