Development of innovative cancer vaccines

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Abstract

Self-adjuvanting vaccines, composed of antigen and adjuvant (immunostimulator) conjugates/co-assemblies, can achieve antigen-specific immune responses. We aim to develop efficient cancer vaccines utilizing this approach. In this study, we designed an artificial enveloped viral replica that presents both the CH401 peptide, a breast cancer antigen, and α-galactosylceramide (α-GalCer, adjuvant) as a novel self-adjuvanting vaccine. The CH401/α-GalCer-displaying enveloped viral replica, prepared via chemical synthesis, effectively induced the CH401 antigen-specific immune responses. A key feature of this vaccine material is its high design flexibility, allowing the co-loading of various immune-modulators with the antigen, thereby enabling precise regulation of antigen-specific immune responses.

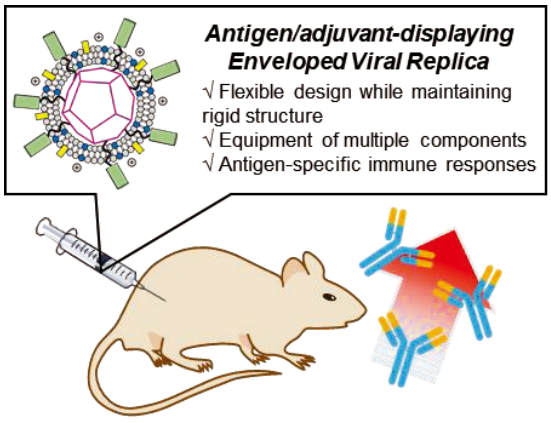
Background & Results

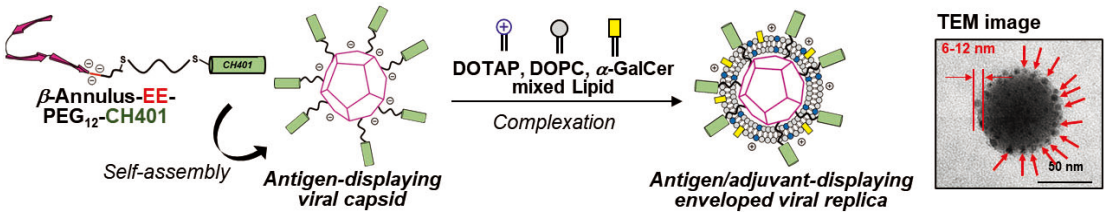
Inactivated vaccines, which is attenuated or killed pathogens, can effectively stimulate immune responses, but are often associated with significant adverse effects. In contrast, subunit vaccines, containing only essential components, offer greater safety but generally exhibit limited efficacy. This research demonstrates that chemically synthesized virus-like particles can effectively induce immune responses. We anticipate that this work will pave the way for the development of next-generation vaccines that merge high safety with robust efficacy.

Significance of the research and Future perspective

Cancer vaccine therapy holds promise for treating inoperable cancers, such as metastatic cancer, and preventing recurrence. However, developing highly effective cancer vaccines remains a challenge due to the immunosuppressive state of cancer patients and the immune evasion mechanisms of cancers. Additionally, there are concerns that overly robust immune responses could lead to serious side effects. Therefore, cancer vaccines have not yet become standard treatment. To address these issues, we are exploring a self-adjuvanting vaccine strategy—a groundbreaking approach where antigens and adjuvants are conjugated or co-assembled to activate the same immune cells, thereby inducing antigen-specific immune responses.

In this study, we developed a self-adjuvanting cancer vaccine using a chemically synthesized artificial virus-like particle as the antigen carrier. The breast cancer antigen, CH401 peptide, was conjugated to a self-assembling peptide from virus-capsid, forming "antigen (CH401)-displaying virus capsid." Encapsulation of these particles into lipid bilayer containing the glycolipid adjuvant α-GalCer produced the "antigen (CH401)/adjuvant (α-GalCer)-displaying enveloped viral replica." This vaccine material demonstrated high stability, efficient uptake by immune cells, and, upon immunization to mice, successfully induced the CH401 antigen-specific immune responses. Therefore, the antigen/adjuvant-displaying enveloped viral replica represents promising vaccine platform capable of eliciting potent and selective immune responses against the target antigen.





Patent
Treatise Manabe, Yoshiyuki; Fukase, Koichi; Matsuura, Kazunori et al. Antigen/adjuvant-displaying enveloped viral replica as a self-adjuvanting anti-breast-cancer vaccine candidate. J. Am. Chem. Soc. 2023, 145(29), 15838-15847. doi: 10.1021/jacs.3c02679
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