Qß1-VLP based anti-fungal peptide vaccines induce robust immunity

Improved Immune Response and Efficacy

Introduction

Conjugating peptides, glycans, and polysaccharides to carrier proteins is an effective way to enhance their immunogenicity. Only a few carrier proteins are used in licensed vaccines, including tetanus and diphtheria toxoids and CRM_{197}, a genetically detoxified diphtheria toxin. *Bacteriophage Qß1 virus-like-particle (Qß1-VLP)* is a promising and novel carrier protein with several potential advantages over traditional protein carriers (Figure 1).

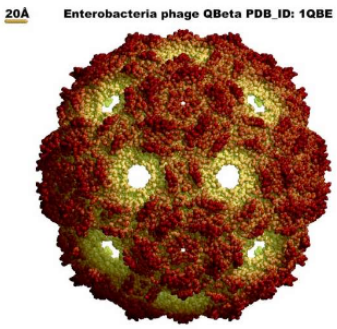


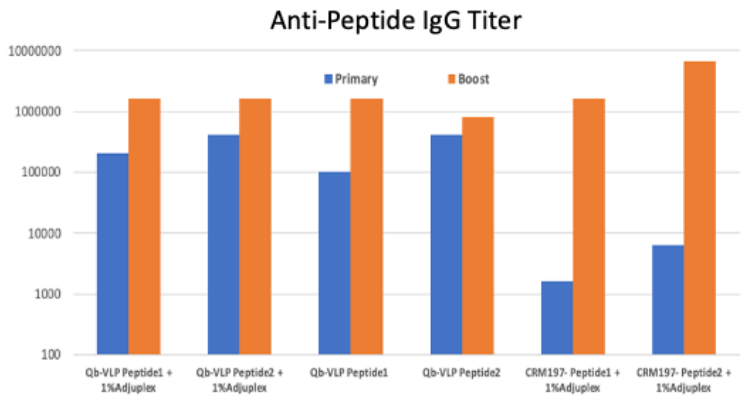
Figure 1. Bacteriophage Qβ1 virus-like-particle (Qβ1-VLP)

- 28 nm particle, composed of hundreds of subunits
- High hapten loading capacity
- Rationally engineered to reduce anti-VLP response
- Efficiently taken up by antigen presenting cells
- Self-adjuvanting as particle incorporates small amounts of nucleic acid during expression and

A Candida Peptide Conjugate Vaccine

Candida is an emerging antibiotic resistance threat and there is no anti-fungal vaccine for humans, as yet. We have identified protective peptide epitopes located on the cell surface of medically important *Candida* species, including MDR C. auris. Inducing suitable immunity with short peptides is challenging since both high antibody titers and a mixed Th1/Th2 immune response are critical for protection against disseminated candidiasis. Two peptides have been identified which, using a peptide-pulsed dendritic cell-based vaccine strategy, induced a protective immune response, in mice, against disseminated candidiasis). However, developing a clinically relevant and effective *Candida* peptide vaccine requires a suitable delivery platform. Here we compared CRM_{197} and Bacteriophage Qβ1 virus-like-particle (Qβ1-VLP) as carrier proteins for Candida-derived peptides.

For this study, two 14-mer peptides, P1 and P2, which our prior studies have shown to induce protective antibodies were each conjugated Qβ1-VLP or CRM_{197} and their immunogenicity compared in mice, with and without Adjuplex™. Adjuplex™ has been shown to function as a potent adjuvant to boost peptide immunogenicity and induce a balanced Th1/Th2 antibody response in mice. Even in the absence of adjuvant, we found that Qβ1-VLP-peptide conjugate increased the immunogenicity of the short peptides by inducing high levels of peptide-specific IgG responses and rapid immunity memory following only one primary immunization (Figure 2). After the 2nd dose, however, the CRM_{197} conjugates had comparable responses as the VLP conjugates. Notably, the peptide-Qβ1-VLP conjugates elicited a more balanced Th1/Th2 immune response than the CRM197 conjugates, as evidenced by the IgG2a to IgG1 ratio (Figure 3), a factor that could be critical for protection against the disease.



- Primary anti-peptide titers were higher for VLP conjugates than for CRM197 but were comparable on boosting.
- Adjuvant did not help response to VLP conjugates

Figure 2. Head-to-head comparison showed the superiority of Qβ1-VLP as peptide carrier vs CRM_{197}. After primary immunization, enhanced anti-peptide specific IgG responses were induced by Qβ1-VLP-peptide vaccine platform as compared to CRM_{197}-peptide conjugates. Robust peptide-specific IgG were comparable after 1st booster for both Qβ1-VLP-peptide and CRM_{197} peptide vaccines.

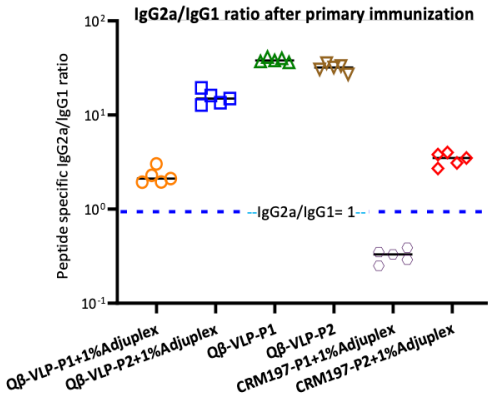


Figure 3. Qß-VLP-peptide conjugates induced balanced or Th1-biased Th1/Th2 immune responses. In the presence of Adjuplex™, Qß-VLP-peptide induced enhanced Th1 biased mixed Th1/Th2 (IgG2a/IgG1) responses were induced vaccines as compared to CRM_{197}-peptide conjugates. In the presence of AS03, Qß-VLP-peptide vaccines induced more balanced Th1/Th2 immunity and CRM197-peptide vaccine induced more Th2 biased Th1/Th2 mixed immune responses.

Conclusion

These studies support the further development of Qβ1-VLP as a carrier protein for peptide vaccines targeting Candida cell surface epitopes and potentially preventing invasive candidiasis. Active immunotherapy is an ideal approach to protect vulnerable immunocompromised populations that have unacceptable mortality, even with appropriate antifungal treatment.

FinaBio is a conjugate vaccine research and development company, providing reagents and technology along with laboratory and consulting services. We are known for our expertise in protein-polysaccharide conjugation. FinaBio also offers a portfolio of carrier proteins, including CRM_{197} and Qβ1-VLP. To learn more about FinaBio, visit www.FinaBio.com or email Info@FinaBio.com

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