CASE STUDY

COMPARABLE IMMUNOGENICITY OBSERVED IN PEPTIDES COUPLED TO PFENEX CRM197 AND KLH IN A MURINE MODEL

In this case study, 3 peptides (peptides #5, #6, and #7) directed to one therapeutic target were conjugated to either Pfenex's CRM197 (a non-toxic diphtheria toxin mutant) or to KLH (keyhole limpet hemocyanin). To allow comparison of the immunogenicity of the resulting formulation, 3 different doses of each formulation were injected (low dose, medium dose, high dose). Three immunizations were given to female BALB/c mice in two-week intervals via the subcutaneous route. Serum was then collected 2 weeks after each injection and antibody titers were determined by ELISA.

Focus of Analysis:

- Kinetics of immune response (based on high dose formulations)
- Magnitude of immune response (antibody titers after 3 immunizations)

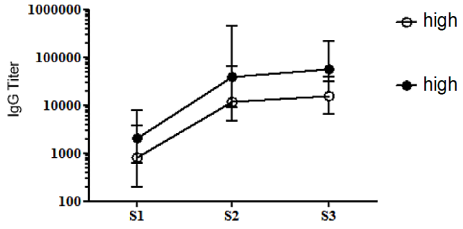
Vaccine Design:

Peptides with ≥95% purity were used. Peptide-CRM197-conjugates and peptide-KLH-conjugates were prepared using the same linker. Conjugates were adsorbed to an adjuvant.

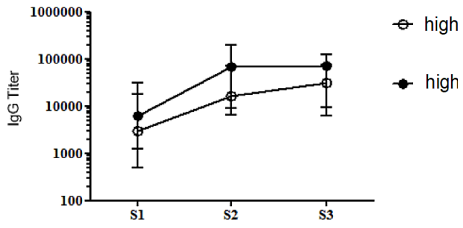
ELISA titers to injected peptides after 1 (S1), 2 (S2), and 3 (S3) immunizations with the highest dose, median with range, n=10 are shown below, left. Titers to injected peptides at S3, single sera and median with range, n=10 are shown below, right.

Immunogenicity in terms of kinetics and magnitude of CRM197 was determined based on 3 different peptides directed to one therapeutic target. Although differences were observed for some doses and peptides, the overall immunogenicity and kinetics of the immune responses were comparable between peptide-KLH and peptide- CRM197 conjugate vaccines in the tested animal model. This experiment provided the data necessary to support the substitution of KLH for Pfenex's cGMP CRM197 in further clinical studies of this vaccine.

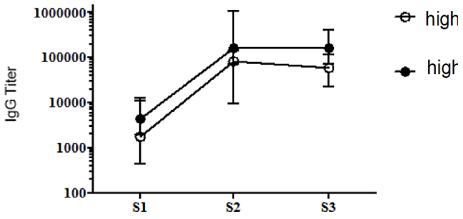
ELISA TITERS TO PEPTIDE #5



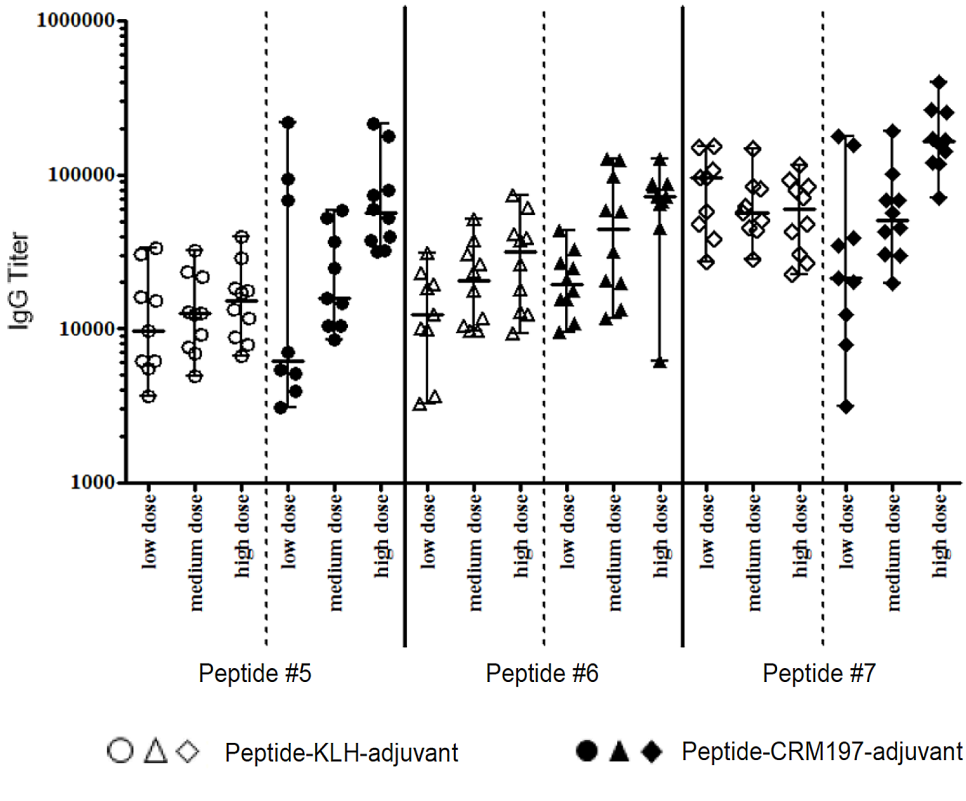
ELISA TITERS TO PEPTIDE #6



ELISA TITERS TO PEPTIDE #6



ELISA TITERS AFTER 3 IMMUNIZATIONS AT ALL DOSE LEVELS



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