

Antibody Responses to Melanoma Helper Peptide Vaccines May Enhance Antigen Opsonization and Presentation

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Vaccination with 6 melanoma “helper” peptides (6MHP) induces both CD4+ T cell and IgG antibody (Ab) responses which are associated with improved survival in melanoma patients. We hypothesized that Abs to 6MHP would bind multiple epitopes on vaccine peptides, forming large antigen-Ab immune complexes (IC) and incorporating complement C1q.

Patients were vaccinated with 6MHP and incomplete Freund’s adjuvant (IFA, n=10), IFA+ polyICLC (n=5), IFA+metronomic cyclophosphamide (mCy, n=5), or IFA+polyICLC+mCy (n=10). Abs to overlapping fragments of vaccine peptides were detected with ELISA. Serum Ab titers were determined at peak IgGtotal response. Positive Ab response was defined as reciprocal titer above 100. Vaccine-site biopsies were evaluated by immunofluorescence.

IgG Abs to 6MHP were identified in 27/30 patients (90%), with 73% and 37% of patients having positive IgG3 and IgG1 titers, respectively. IgG2 and IgG4 responses were not observed. Adding polyICLC to IFA significantly increased IgGtotal (p=0.004) and IgG3 (p<0.001) titers (Figure 1). Adding mCy did not enhance IgG responses. Serum Ab responses were detected to overlapping fragments of vaccine peptides, and both IgG and C1q were detected in vaccine sites.

These data provide evidence that 6MHP vaccination induces memory B cells which undergo isotype switching, producing IgG subtypes that facilitate antigen opsonization. These data also suggest that 6MHP peptides contain overlapping epitopes that could allow Abs to form ICs, triggering complement activation in vaccine sites. Finally, these data also show that adjuvant polyICLC enhances Ab responses. Future studies will investigate whether peptide-antigen presentation is enhanced by these class-switched Ab responses.

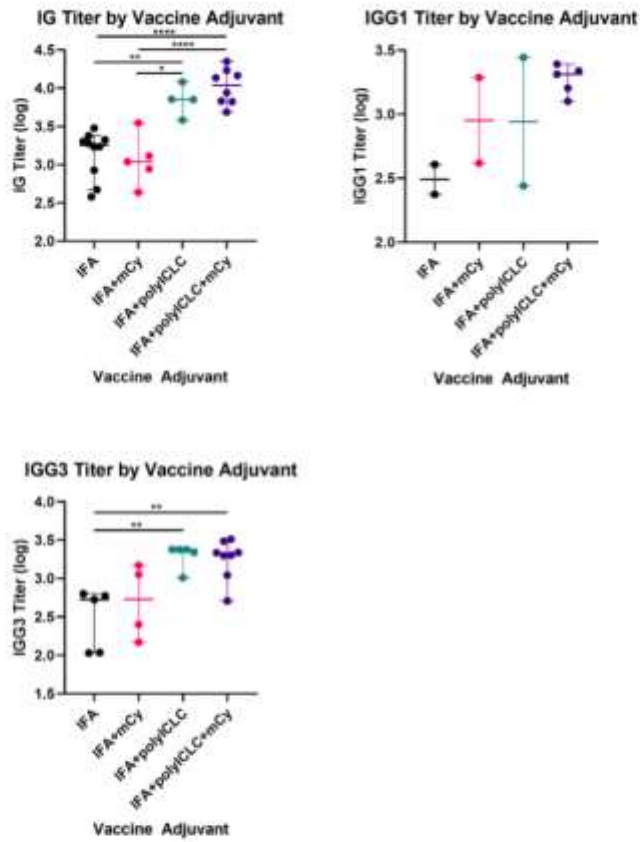


Figure 1: Induction of IgG response to 6MHP by adjuvant regimen. **** = p value <0.0001, ** = p value <0.01, * = p value <0.05. P values calculated using Tukey's range test.