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Poster presentation

P05-07. Evaluation of peripheral and bone marrow B cell responses in rhesus macaques after immunization with soluble HIV-1 gp140 trimers

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Background

Broadly neutralizing antibodies (bNAbs) against HIV-1 are not efficiently elicited by vaccination despite considerable efforts. bNAb elicitation is likely limited both by current envelope glycoproteins (Env) immunogens, which are not sufficient mimics of the native Env spike complex, and by the lack of immunization regimens that promote optimal development and maturation of B cell responses. So far, analyses from protein immunization studies focus mainly on serological antibody responses and less on responses at the B cell level. Here, we characterize frequencies of antigen-specific antibody secreting cells (ASC) and memory B cells in the periphery and bone marrow of rhesus macaques immunized with soluble gp140 trimers. These analyses provide a foundation for the design of improved immunization protocols to elicit bNAbs against HIV-1.

Methods

We established stimulation protocols for *in vitro* expansion and differentiation of macaque memory B cells into ASC to allow enumeration and monitoring of memory B cells post immunization. Using a series of variant Env probes, the frequencies of B cells specific for different structural determinants of Env were quantitated by B cell ELISpot analysis.

Results

By stimulating peripheral PBMCs with a mitogen cocktail we detected Env-specific memory B cells at a sensitivity of ~0.1% of the total number of memory cells. By sampling peripheral PBMCs at several time points after soluble gp140 trimer immunization we demonstrate that ASC peak one week after immunization while memory B cell responses peak between one and two weeks after immunization. The peripheral gp140-specific memory B cell pool constitutes between 10 to 20% of the total peripheral memory B cell pool.

Conclusion

By establishing *in vitro* stimulation protocols for rhesus memory B cells, and determining the peak of antigen specific responses after protein vaccination, we describe a benchmark study that can be used to inform future analyses of vaccine-elicited B cell responses in primates.