Abstract Preview - Step 3/4

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Topic: Novel vaccine and prevention concepts

Title: Optimisation of *Ex Vivo* Memory B Cell Expansion/Differentiation for Interrogation of Rare Subsets in Response to Effective vs Ineffective Vaccination

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Text: **Background:** Successful vaccines typically induce long-lived B cell memory responses that are maintained for decades. In contrast current HIV-1 vaccines generate poor long-term memory B cell responses. Peripheral memory B cells are rare, particularly in the setting of vaccine-generated responses, necessitating *in vitro* expansion to elucidate the nature and degree of humoral response. Using a structured design of experiments (DoE) approach we sought to determine the optimal memory B cell expansion conditions and characterise the resultant cells by flow cytometry and IgH sequencing, methodology that will allow a comprehensive assessment of vaccine-reactive cells generated by effective licensed and trial vaccines.
Methods: Optimal memory B cell expansion conditions were determined using a DoE wide screen of various iterative combinations of cytokines, TLR, and CD40L stimulation. Total Ig (IgG, IgM & IgA) cellular secretion was determined by ELISA. Cell expansion/differentiation was tracked using flow cytometry with cell trace violet and by IgH sequencing.
Results: Following a screen of 9 stimulants, totaling over 300 conditions, we identified a combination of IL-21, CpG ODN_{2006}, R848 and CD40 stimulation as being optimal for the induction of expansion and differentiation of memory B cells into antibody secreting cells. The optimized stimulation cocktail is capable of inducing 2,000 memory B cells to secrete up to 80 mg of total Ig (IgG, IgA & IgM). Phenotypical analysis showed that memory B cells undergo up to 6 rounds of division and adopt a “plasmablast” phenotype by the end of a 10-day culture period.
Conclusions: To date such a wide systematic screen and characterization of *ex vivo* memory B cell expansion/differentiation has not been reported; we now aim to use this work to investigate potential developmental blocking points in memory B cell subset responses between effective licensed vaccines and the current generation of HIV-1 clinical trial vaccines.

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