Impact of aging, RhCMV infection and SIV infection on circulating B cell dynamics

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Background: Mechanisms for B cell alterations resulting from aging, chronic virus infections including rhesus cytomegalovirus (RhCMV) and acute viral infections such as simian immunodeficiency virus (SIV) have not been thoroughly examined in rhesus macaques. However, aging, human CMV, and human immunodeficiency virus (HIV)-1 have proven to impact humoral responses to new pathogens and vaccines in humans and warrant investigation in rhesus macaques.

Materials and Methods: Multiparameter FACS analysis was used to distinguish naïve and different memory B cell subsets in Specific Pathogen Free (SPF) and non-SPF macaques for ages spanning one to 30 years. Circulating memory B cell subset changes associated with chronic viral infection were determined by comparison of non-SPF and SPF macaque cohorts. B cell subsets in blood were assessed longitudinally in macaques experimentally infected with either RhCMV or SIVmac251. Dynamics of antibody development and avidity during acute and early chronic RhCMV and SIV infections were correlated with memory subset frequencies. Statistical analysis included Mann-Whitney nonparametric test and Spearman correlation.

Results and Conclusions: Significant differences in B cell subsets were noted between ages one to five years for both SPF and non-SPF macaques. Interestingly, changes in B cell subsets observed over a span of five to 30 years were unique to those observed for childhood to young adult. Significant differences in B cell subsets noted in non-SPF compared to SPF macaques matched subset changes observed during acute and early chronic experimental RhCMV infection. Typical progressor SIV infections induced SIV-specific IgG responses characterized by poor avidity, increases in circulating B cell counts, declining plasma RhCMV antibody concentrations, and increased activated memory B cells coincident with decreases in resting memory and naïve B cell frequencies similar to B cell alterations reported for HIV-1 infection.

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