Retrovirology

Poster presentation

P16-26. High avidity virus-specific CD4+ T cells are lost during retroviral infection due to interaction with B cells

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Background

Retroviruses can establish persistent infection despite induction of an antiviral immune response. We have previously shown that immune resistance to retroviral infection of mice with Friend Virus (FV) is overcome by B cell activation, triggered by microbial products or coinfection with Lactate dehydrogenase-elevating virus (LDV). Here we examined the contribution of FV-specific CD4+ T cells to protection against infection and disease, and the involvement of B cells in shaping the virus-specific CD4+ T cell response.

Methods

To correlate cytokine environment with B cell activation and FV-induced disease enhancement by coinfection, we have used 23-plex assays and IFNγR knockout mice. Kinetics and clonal composition of FV-specific CD4+ T cells, as well as their protective value against infection, were evaluated following adoptive transfer into resistant ($Fv2^r$) or susceptible ($Fv2^s$) hosts, with varied antigen presenting cell composition. To do so, we have developed a TCRβ transgenic mouse with a polyclonal repertoire of FV-specific CD4+ T cells.

Results

High-avidity FV-specific CD4+ T cell clones preferentially expanded during acute FV infection and dominated the early response, but were subsequently replaced by low avidity clones. LDV coinfection, which led to polyclonal B cell activation, accelerated the loss of high-avidity FV-specific CD4+ T cell clones. Furthermore, enhancement of FV replication and disease by LDV coinfection was associated with early pro-inflammatory type I and II interferon responses. Genetic depletion of B cells dramatically altered the clonal composition of FV-specific CD4+ T cells and prevented the loss of high-avidity clones. Moreover, an increased frequency or constant supply of FV-specific CD4+ T cells was both necessary and sufficient to prevent or contain FV infection, even in the face of coinfection.

Conclusion

We show an unappreciated protective effect of virus-specific CD4+ T cells against retroviral infection and reveal the influence of B cells on the clonal composition of the CD4+ T cell response.