Retrovirology

Poster presentation

P03-05. CD4 targeted vaccination in retroviral infection

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Background

Retroviruses are able to establish persistent infection despite induction of a multipartite antiviral immune response. Whether collective failure of all parts of the immune response or selective deficiency in one crucial part underlies the inability of the host to resist retroviral infection is currently unclear.

Methods

Here we examine the contribution of the virus-specific CD4+ T cells in protection against Friend virus (FV) infection in the murine host. We have developed a TCR-β transgenic mouse with a polyclonal repertoire of CD4+ T cells, which we adoptively transfer into a variety of different hosts, with distinct genetic susceptibility or lymphocyte composition.

Results

We show that the magnitude and duration of the FV-specific CD4+ T cell response is directly proportional to resistance against acute FV infection and subsequent disease, demonstrating a previously unappreciated protective role. Notably, significant protection against FV-induced disease is afforded by FV-specific CD4+ T cells in the absence of a virus-specific CD8+ T cell or B cell response. Enhanced spread of FV infection in hosts with increased genetic susceptibility or during coinfection with lactate dehydrogenase-elevating virus (LDV) causes a proportional increase in the number of FV-specific CD4+ T cells required to control FV-induced disease. Furthermore, ultimate failure of FV/LDV coinfected hosts to control FV-induced disease is accompanied by accelerated contraction of the FV-specific CD4+ T cell response. Conversely, a further increased frequency or constant supply of otherwise naïve FV-specific CD4+ T cells is both necessary and sufficient to effectively contain acute infection and prevent disease, even in the presence of coinfection.

Conclusion

Thus, these results suggest that FV-specific CD4+ T cells provide significant direct protection against acute FV infection, the extent of which critically depends on the ratio of FV-infected cells to FV-specific CD4+ T cells.