

The Epstein-Barr Virus-Host Interaction ... so many experiments and still so much to learn!!

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Infection with Epstein-Barr virus (EBV) can lead to the acute self limiting illness infectious mononucleosis which is characterised by the massive expansion of EBV-specific CD8⁺ T cells, which contract with the resolution of the acute disease. We have used this infection as a model to study the generation, maintenance and distribution of CD8⁺ T cell immunity to EBV during primary infection into chronic carriage of this virus. We have found when tracking CD8⁺ T cell responses made during primary infection that not all specificities present in the primary response are maintained long term. Thus of three well characterised HLA-A2 restricted reactivities present in the primary EBV response, we find that two are efficiently maintained into memory while the third is not, even when it is initially the dominant specificity. This is despite the absence of any obvious differences in differentiation status and function between the T cells. Interestingly the specificity which is lost shows a dramatic upregulation of the IL-7 receptor-alpha, suggesting loss of antigen stimulation with this epitope, as well as a distinct upregulation of the surface marker programmed death-1, PD-1, prior to its disappearance. This latter marker has been associated with exhaustion of cells in uncontrolled chronic infection. In the case of a well controlled infection such as that caused by EBV, high expression of PD-1 identifies an individual epitope response that, though still apparently functional, is destined to disappear.