

The dual role of CD27-signalling in viral infections

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CD27 is a member of the tumor necrosis factor receptor (TNFR) family. Interaction with its transmembrane ligand CD70, which is expressed on activated T and B cells and on subsets of dendritic cells, induces a costimulatory signal that promotes survival, enhances T cell receptor (TCR)-mediated proliferative signals, and increases effector function. CD70 is over-expressed in HIV-infected patients and in patients with cancer. Persistent signaling to CD27⁺ effector cells might either lead to improved T cell function or to T cell dysfunction.

Comparable to HIV and EBV infection in humans, memory CTL after infection with lymphocytic choriomeningitis virus (LCMV) in mice retained CD27 surface expression. We found that LCMV-specific memory CTL generated in the absence of CD4⁺ T cell help or in the absence of B cells are CD27^{low}. The functional role of CD27 expression during the initial priming and on memory CTL was analyzed in CD27-deficient mice. After infection with LCMV, primary CTL responses and the generation of a stable frequency of memory CTLs was comparable in CD27^{-/-} and control mice. In contrast, protective CTL memory against a direct challenge infection with Vacc-G2 was impaired in the absence of CD27 and CD27^{-/-} memory CTL protected less efficiently in adoptive transfer experiments. Analysis of LCMV gp33-specific CTL from CD27^{-/-} and C57BL/6 mice revealed that autocrine IL-2 production and secondary expansion was impaired in the absence of CD27 signaling. These results suggest that CD4⁺ T helper cells and polyclonally activated B cells imprint the capacity of autocrine IL-2 production and secondary expansion via regulation of CD27 expression on memory CTL.

Antibody responses to non- or poorly cytopathic viruses such as LCMV infection in mice and HIV and hepatitis C virus (HCV) in men are usually weak and slow to develop. We found that during LCMV infection, persistent CD27 signaling causes a CD4⁺ T cell-dependent destruction of the splenic architecture and a functional immunodeficiency with reduced and delayed virus-specific antibody responses. This acquired immunosuppression allows the virus to establish a persistent infection.

Therefore, in some situations CD27 signalling improves T cell responses whereas in others it has detrimental consequences on host immunity. This difference may depend on the amount, duration, and timing of the CD70 signal provided.