

The FADD/Caspase-8 pathway regulates the antigen-induced expansion of CD8⁺ but not CD4⁺ T cells

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FADD is a molecular adaptor required to link “death receptors” to the cell-extrinsic apoptotic pathway. To study this pathway of “death receptor” signaling, mice expressing a dominant negative form of FADD (FADD^{dd}) in T cells were generated in our lab. The T cells from such mice were shown to have a defect in Fas-induced apoptosis, but surprisingly, the same T cells also exhibited a block in t activation-induced proliferation. In order to further characterize the role of FADD in the proliferative response, we have bred FADD^{dd} mice to mice expressing both MHC class I-restricted and MHC class II-restricted T cell receptor (TCR) transgenes. As expected, FADD^{dd} mice with an MHC class I TCR transgene reveal a profound block in their proliferative response to antigen, despite normal early activation status and IL-2 production. However, FADD^{dd} mice with an MHC class II TCR transgene have a normal proliferative response to antigen. Additionally, FADD^{dd} transgenic mice are severely deficient in response to an LCMV challenge. Our recent experiments have been designed to illuminate the specific pathways emanating from FADD that can also modulate cell survival and successful completion of the cell cycle.