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γδ T cells of the immune system respond to stressed or dying cells

γδ T cells are involved with the host response to infection and autoimmunity. Unlike conventional αβ T cells, traditional MHC-restricted recognition of γδ ligands has not been identified. Furthermore, few γδ ligands have been verified and the conditions under which these ligands are induced remain ill-defined. γδ T cell activation is induced indirectly via dendritic cell (DC) activation by the Lyme spirochete, *Borrelia burgdorferi,* through TLR2. The Budd laboratory has observed that caspase-8 promotes murine DC survival via cleavage of RIPK1, inhibiting formation of the death-inducing ripoptosome. Caspase inhibition in bone marrow dendritic cells (BMDC) by the pan-caspase blocker, zVAD, leads to cell death but, paradoxically, also to increased activation of γδ T cells. BMDC exposed to the cytokine IL-4 upregulate c-FLIP, a stabilizer of caspase-8 activity, which renders them rather resistant to cell death by zVAD. Interestingly, IL-4-treated BMDC also display a decreased ability to activate γδ T cells, suggesting a model for induction of γδ ligand expression by death of BMDC. My studies have extended these findings to human DC and γδ T cells. One caveat is that human DC appear to be less sensitive to caspase inhibition than their murine counterparts, with nearly a ten-fold increase in exposure to zVAD necessary to induce cellular death. In short, cell death of DC may be a necessary factor for γδ T cell ligand expression, suggesting a role for γδ T cells in the immune surveillance of cell stress.