Newborns typically have immune responses that are allergic, due to a predominance of Th2 cells, and lack the ability to respond to vaccines as well as display poor protection against microbes, due to a lack of Th1 cells. Our lab has previously discovered that the paucity of Th1 cells in the neonatal period occurs because these cells die during a second antigen encounter. This research utilizes murine neonates to demonstrate that Th1 cell death occurs from antigen and IL-4/IL-13 cytokine signaling and identifies the signaling pathway within the cell that leads to death. Interestingly, a novel role for a transcription factor, interferon regulatory factor 1 (IRF-1), has been discovered whereby it is induced upon cytokine signaling and initiates the intrinsic apoptosis pathway. Furthermore, by blocking this pathway, it is possible to rescue neonatal Th1 cells and improve vaccine efficacy in newborn mice. This is of high clinical importance as a significant number of human neonatal deaths occur from infections and vaccines remain at the forefront of infection prevention.