Liver-primed memory T cells generated under noninflammatory conditions provide anti-infectious immunity.

Development of CD8(+) T cell (CTL) immunity or tolerance is linked to the conditions during T cell priming. Dendritic cells (DCs) matured during inflammation generate effector/memory T cells, whereas immature DCs cause T cell deletion/anergy. We identify a third outcome of T cell priming in absence of inflammation enabled by cross-presenting liver sinusoidal endothelial cells. Such priming generated memory T cells that were spared from deletion by immature DCs. Similar to central memory T cells, liver-primed T cells differentiated into effector CTLs upon antigen re-encounter on matured DCs even after prolonged absence of antigen. Their reactivation required combinatorial signaling through the TCR, CD28, and IL-12R and controlled bacterial and viral infections. Gene expression profiling identified liver-primed T cells as a distinct Neuropilin-1(+) memory population. Generation of liver-primed memory T cells may prevent pathogens that avoid DC maturation by innate immune escape from also escaping adaptive immunity through attrition of the T cell repertoire.