



## 13. T cells IV: Cytotoxicity and innate-like lymphocytes

Learning objectives and summary

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### Learning objectives:

1. Understand how CD8 cytotoxic T cells (CTLs) kill targets via interactions with targets bearing MHC Class I molecules loaded with viral peptides. Understand the individual roles of granules and FasL in CTL-mediated killing.
2. Be able to explain the mechanism of “cross-priming” and describe its role in viral immunity.
3. Don't forget memory cells.
4. Appreciate the roles that innate-like B lymphocytes (B1 cells, marginal zone B cells) play in the immune system.
5. Learn the functions of innate-like T lymphocytes (NK cells,  $\gamma\delta$  T-cells, and NK T cells) in the immune system.

### SUMMARY

1. For cytotoxic CD8 T-cells, ligation of the TCR by MHC I/peptide + co-stimulation results in release of granzymes and perforin and/or FasL, leading to apoptosis of the target cells.
2. Viruses evade host defense, in part, by down-regulating MHC Class I. Uninfected dendritic cells circumvent this by “cross-priming”: phagocytosis of virus-infected cell and presentation of “exogenous” viral antigens on MHC Class I.
3. CD8 T cells can function without CD4 help, but need CD4 help to develop into effective memory cells. CD4 memory cells live for years; central memory cells home to lymph nodes and effector memory cells home to inflamed tissue.
4. NK cells lack TCRs, but instead express both activating and inhibitory receptors (killer inhibitory receptors, or KIRs). KIRs contain ITIMs and recruit phosphatases that inhibit NK cell functions. The relative expression and ligation of these receptors determines the outcome (i.e., killing or not) of the NK effector response.
5. KIRs on NK cells bind to MHC Class I molecules on healthy cells and thus tonically inhibit their activity. Downregulation of MHC Class I by viruses relieve KIR-mediated repression and viral-induced expression of MICA and MICB, which bind activating receptors on NK cells, lead to lysis of virally-infected cells.
6. Innate immune B-cells (e.g., B-1 cells and marginal zone B cells) recognize carbohydrate antigens, secrete IgM, and are not long-lived.
7. Innate immune T-cells ( $\gamma\delta$  T-cells, and NK T cells) recognize non-peptide antigens bound to non-classical MHC-like molecules. They mediate cytotoxicity, rapid cytokine secretion, and trigger maturation of DCs (and therefore initiate acquired immunity).