NKT Cells: Invariant

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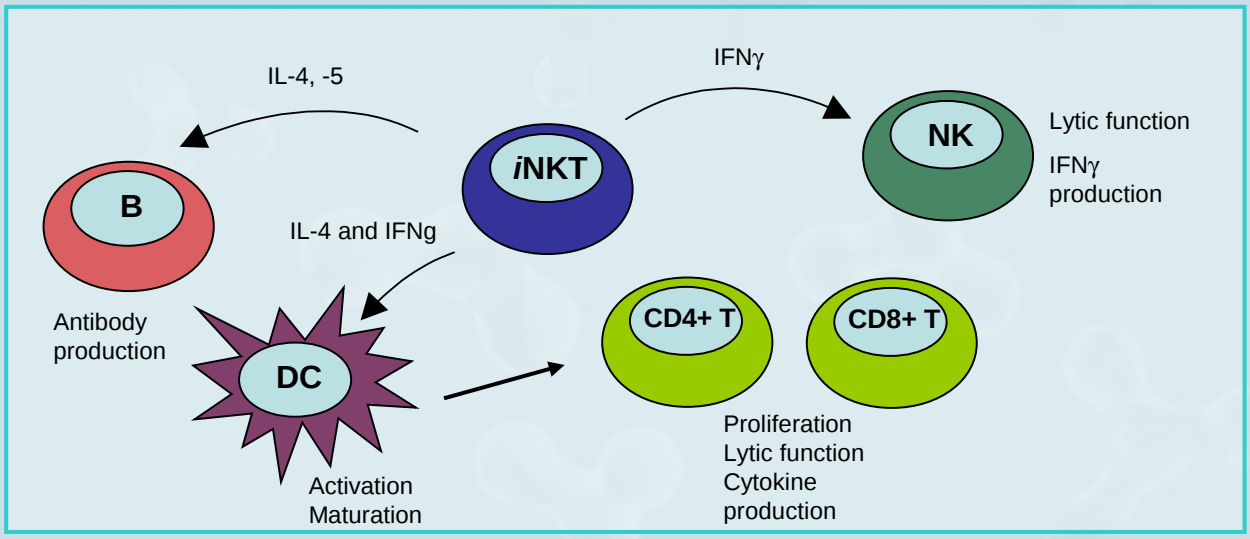
Invariant natural killer T (*i*NKT) cells, also known as type I or classical NKT cells, are a distinct population of T cells that express an **invariant αβ T-cell receptor (TCR)** and a number of cell surface molecules in common with natural killer (NK) cells. Although *i*NKT cells are rare in the human blood pool, comprising just 0.01-1% of peripheral blood mononuclear cells (PBMCs), they are important **immunoregulatory cells** rapidly producing large amounts of cytokines that can influence other immune cells.

Recognition of antigen

*i*NKT cells express a restricted TCR repertoire that, in humans, is composed of a Vα24-Jα18 TCRα chain preferentially coupled with a Vβ11 TCRβ chain. Unlike conventional T cells, which mostly recognise peptide antigens presented by MHC molecules, *i*NKT cells recognise **glycolipid antigens** presented by the **non-polymorphic MHC class I-like molecule, CD1d**. *i*NKT cells are frequently characterised by the recognition of the prototypical glycolipid, α–galactosylceramide (**α-GalCer**), a marine-sponge-derived agent, which also potently activates them and has strong anti-tumour activity.

Immunoregulatory roles

Functionally, human *i*NKT cells can be divided into three subpopulations, which are either **CD4+, CD8+ or CD4- CD8- (DN)**. *In vitro* studies have shown that CD4+ *i*NKT cells tend to produce both **Th1 and Th2-type cytokines** and may have a more immunoregulatory role, while CD8+ and DN *i*NKT cells appear more Th1-like in response and have a stronger **cytolytic ability**. *i*NKT cell-derived cytokines and chemokines can modulate several other cell types, including NK cells, conventional CD4+ and CD8+ T cells, macrophages, neutrophils and B cells as well as recruiting and activating dendritic cells.



Some examples of the interactions of *i*NKT cells with other cell types

Role in disease

*i*NKT cells have been implicated to play a role in a number of immune-related diseases. Their multi-functional responses have been shown to enhance microbial and tumour immunity as well as suppressing autoimmune disease and promoting tolerance. However, *i*NKTs have also been shown to exacerbate certain other diseases such as allergy. There are many ongoing clinical studies that hope to exploit the **potential immunotherapeutic properties** of *i*NKT cells.