



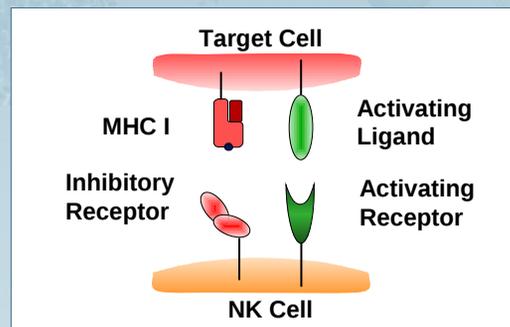
Natural Killer Cells

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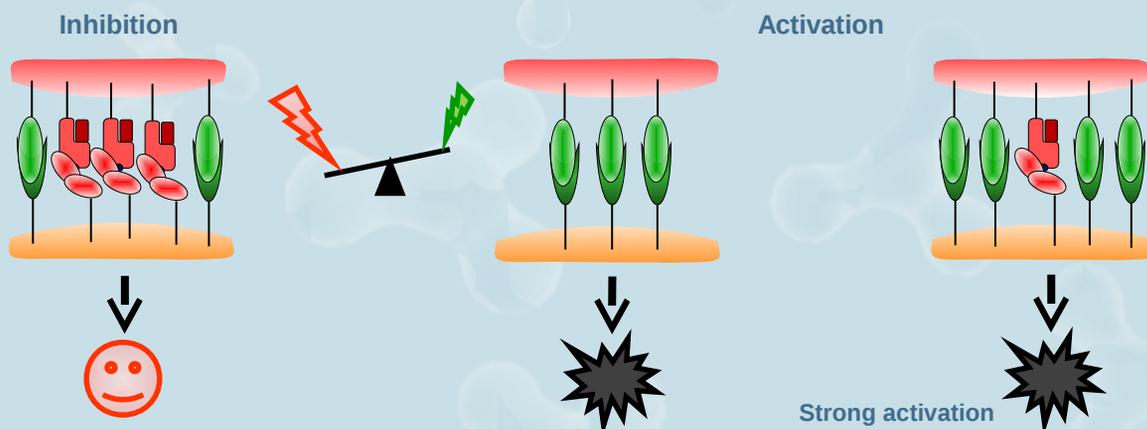
Natural Killer (NK) Cells represent one of the three subsets of lymphocytes, besides T- and B-cells. In comparison to the latter, NK cells belong to the **innate immune system** and form a first line of defence against a wide variety of pathological challenges. Particularly, they provide protection against viral and bacterial infections and they help to detect and limit the development of cancer.

In this regard, NK cells were first described as cells that have the ability to kill tumour cells without any priming or prior activation (remember that e.g. cytotoxic T cells need priming by antigen presenting cells) and their name is ultimately connected to this **'natural' ability to kill**. Additionally, NK cells secrete **cytokines**, as for example INF γ and TNF α , which constitute a second important defence mechanism during an immune reaction.

One could imagine that cells which display a natural ability to kill need to be controlled very strictly to protect healthy cells from attack. Therefore, in addition to a variety of different **activating receptors**, NK cells express **inhibitory receptors** that recognize cognate MHC class I (this is also referred to as recognition of 'self'). This is a very efficient mechanism of control as almost all 'normal' cells express MHC class I and are therefore protected from unwanted attack.



While on patrol NK cells constantly contact other cells. During these interactions a balance of activating and inhibitory signals determines whether NK cells attack or not.



Strong inhibition

Healthy, 'normal' cells express enough **MHC class I molecules** to induce a strong inhibitory signal in NK cells. These cells are therefore protected from NK cell attack.

Reduced inhibition

Tumour cells or cells infected by viruses often **downregulate MHC class I** molecules. These cells can no longer deliver a strong inhibitory signal. NK cells will therefore attack and eliminate these cells.

Strong activation

Transformed or infected cells sometimes **increase the expression of molecules that are recognised by activating NK cell receptors** (activating ligands). NK cells now receive a much stronger activating signal than usually. This may override the inhibitory signal and allow NK cells to attack.