

Co-Receptors: Function

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The activation of specialised immune cells from the adaptive immune response (i.e. **B cells** and **T cells**) is controlled by their specific antigen receptor but also by co-receptors.

T cell co-receptors

In order to be fully activated and ready to respond to intruders or damaged cells, naïve T cells (that haven't contacted antigen) need to be activated by two signals. The first one is from the **T-cell receptor (TCR)**. As the TCR recognises a small part of the antigen (called peptide), this ensures the specificity of the response; only T cells that recognise this antigen will be activated. The second signal (called signal 2 or co-stimulatory signal) is provided by a **costimulatory molecule**. The better characterised one is **CD28**, among others (**ICOS**, **OX40**, **CD46**...). Without receiving a second signal, the T cells remain mainly unresponsive, becoming **anergic** cells, or die. Cleverly, most of the ligands for these costimulatory molecules are induced by activation/maturation of the cells that present the peptide to the T cells (called **antigen presenting cells**, APC). When the APCs see an antigen and cut it into peptides for presentation in a complex with MHC molecules to activate T cells, they also upregulate the ligands for some of these costimulatory molecules, rendering them able to activate the specific T cells. For example, the ligands of CD28 (**B7-1** and **B7-2**, also called **CD80** and **CD86**) are induced on APCs and allow activation of CD28 on the T cells.

As one does not want continuous **T-cell activation**, there is also another set of co-receptors which inhibit T-cell activation. They are called **co-inhibitory receptors**, and include **CTLA-4** and **PD-1**. These molecules are only expressed on T cells that have already been activated. Stimulation of these induced co-inhibitory receptors will curtail T-cell activation, and therefore contribute to a balanced immune response. Indeed, defects in these co-inhibitory receptors lead to aberrant immune responses, such as lymphoproliferation and autoimmunity.

The roles of co-stimulatory and co-inhibitory receptors in T cell activation are illustrated in **Figure 1**.

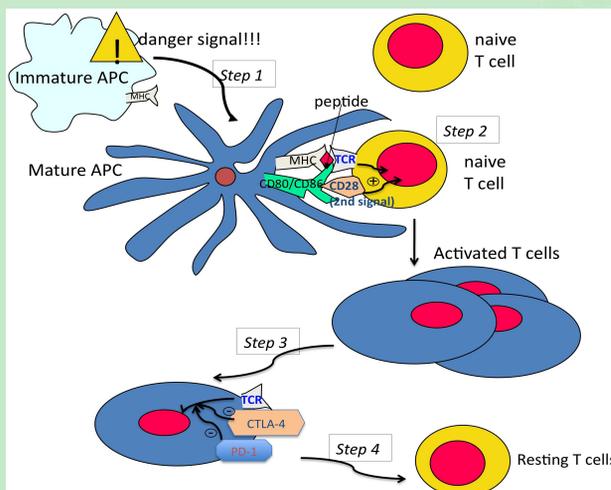


Figure 1. T cell activation is controlled by co-stimulatory and co-inhibitory receptors. The adaptive immune response starts when an antigen presenting cell (APC) recognises a danger signal (virus, bacteria, damaged self...). This induces its maturation, the cutting of the antigen into small peptides for presentation in a complex with MHC, as well as the induction of ligands of costimulatory molecules (step 1). This allows the recognition of the peptide by the TCR of the specific T cell, and its activation by costimulatory molecules. As a result, T cells proliferate and are fully activated (step 2). Activated T cells then express co-inhibitory receptors (CTLA-4, PD-1) (step 3), which will terminate the T cell response (step 4).

B cell co-receptors

The specific **B-cell receptor (BCR)**, an immunoglobulin molecule attached to the membrane of the B cell) recognises the antigen in native form, as opposed to the TCR that recognises antigenic peptides. Costimulation of B cells is notably achieved by the molecule **CD40**. CD40 ligand is expressed on T cells. As B cells can also present peptides to T cells, there is a dialogue between T- and B cells that allows continuous B-cell proliferation and optimal activation leading to their differentiation into **plasmocytes**, which are mature B cells producing high affinity antibodies against the original antigen.