2.1.2

Thymic Selection

The thymus is located in the upper anterior part of the chest behind the sternum and between the lungs. In the thymus, T-cells go through something called **thymic selection**. Thymic selection is a process that involves antigen presenting cells (APCs) in the thymus interacting with maturing T-cells and causing the selection of which T-cells will continue to survive. This process is important as it will determine which cells become CD8+ cells (cytotoxic T-cells) and which will become CD4+ cells (helper T-cells). This process will also work to eliminate any T-cells that could react and destroy self-antigen presenting cells. Otherwise, T-cells could survive that might attack our own cells and tissues and thus lead to autoimmunity.

Thymic selection involves two processes: positive selection and negative selection. **Positive selection** is where T-cell precursors differentiate into either CD4+ or CD8+ cells. Antigen presenting cells in the thymus present MHC I and MHCII molecules (these are discussed more in section 2.1.3) that are associated with self-peptides. Maturing T-cells will bind via their T-cell receptors (TCRs) to these MHC complexes. T-cells that bind to MHC II receive signals to develop into CD4+ cells, while T-cells that bind to MHC I receive signals to develop into CD8+ cells. T-cells that do not bind well to MHC I or II will perish because a signal passed between the bound cells appears to be necessary for survival. In this way T-cells are “positively” selected for the trait of having cell membrane receptors capable of binding to MHC molecules which will be found in the body tissue or antigen presenting cells later on in their life.

The strength of this MHC to TCR bond is important for the process called **negative selection**. If a T-cell has a TCR that has strong recognition for the self-peptides expressed on the MHC molecules of a thymic antigen presenting cells, then the T-cell will stay bound more tightly and for a longer period of time. If it stays bound too long, an apoptotic signal is passed between the cells and the tightly bound T-cell ends up perishing. This is called negative selection because the cells that have the greatest affinity for recognizing self-antigens receive a “negative” signal and die. Their removal prevents them from causing autoimmune diseases if they were to exit the thymus.

In summary, during thymic positive selection the T-cells that are selected to survive have the ability to participate in immune responses by correctly binding MHC molecules on antigen presenting cells. Negative selection is the destruction of any immunocompetent T-cells that have too strong a recognition of self-peptides. In the end, the cells that leave the thymus have the capability to interact with MHC molecules but not self-peptides. Instead, they are prepared to seek out pathogenic peptides expressed on the MHCs of infected cells or APCs.