

## Induction of primary immune responses

Induction of a **primary immune response** begins when an **antigen** penetrates epithelial surfaces. It will eventually come into contact with **macrophages** or certain other classes of **Antigen Presenting cells (APCs)**, which include **B cells**, monocytes, dendritic cells, Langerhans cells and endothelial cells. Antigens, such as bacterial cells, are internalized by endocytosis and "processed" by the APC, then "presented" to immunocompetent lymphocytes to initiate the early steps of the immunological response. Processing by a macrophage (for example) results in attaching antigenic materials to the surface of the membrane in association with **MHC II** molecules on the surface of the cell. The antigen-class II MHC complex is presented to a **T-helper (TH2)** cell which is able to recognize processed antigen associated with a class II MHC molecule on the membrane of the macrophage. This interaction, together with stimulation by **Interleukin 1 (IL-1)**, produced by the macrophage, will activate the TH2 cell. Activation of the TH2 cell causes that cell to begin to produce **Interleukin 2 (IL-2)**, and to express a membrane receptor for IL-2. The secreted IL-2 autostimulates proliferation of the TH2 cells. Stimulated TH2 cells produce a variety of lymphokines including **IL-2, IL-4, IL-6**, and **gamma Interferon** which mediate various aspects of the immune response. For example, IL-2 binds to IL-2 receptors on other T cells (which have bound the Ag) and stimulates their proliferation, while IL-4 causes B cells to proliferate and differentiate into antibody-secreting **plasma cells** and **memory B cells**. IL-4 activates only B cells in the vicinity which themselves have bound the antigen, and not others, so as to sustain the specificity of the immune response.

As previously mentioned, **B cells themselves behave as APCs**. Cross-linked antigens bound to antibody receptors on the surface of a B cell cause internalization of some of the antigen and expression on the B cell membrane together with MHC II molecules. The TH2 cell recognizes the antigen together with the Class II MHC molecules, and secretes the various lymphokines that activate the B cells to become antibody-secreting plasma cells and memory B cells. Even if the antigen cannot cross-link the receptor, it may be endocytosed by the B cell, processed, and returned to the surface in association with MHC II

where it can be recognized by specific TH2 cells which will become activated to initiate B cell differentiation and proliferation. In any case, the **overall B-cell response leads to antibody-mediated immunity** (AMI).