Antigen presenting cell (apc): structure and function

There are many complex mechanisms employed by the immune system to destroy invading organisms, abnormal cells and contain infections in order to maintain health and life. Antigen presenting cells (APC) are some of the cells that form part of these mechanisms. This essay will look at what APCs are, the different types with examples and their specific roles in the immune response.

APCs are cells that take up antigens and present them to lymphocytes during an immune response (Sherwood et al, 2009). The components of APCs that actually do the presenting are Major Histocompatibility complexes (MHCs): Class I and Class II MHC molecules (Sompayrac, 2003). These two complexes provide two different pathways of antigen presentation that stimulates different population of T cells to eliminate the invading pathogen concerned.

All nucleated cells of the body express MHC class I molecules and are therefore referred to as non-professional APCs (Kropshofer et al, 2005). MHC class I molecules are like ‘ billboards’ that display on the surface of the cell, peptides of processed endogenous proteins (Sompayrac, 2003). The endogenous proteins could be those encoded by viruses or parasites that have infected the cell. The main focus of MHC class I APCs is on events within the cell. Typically in a viral infection, the virus enters the cell and uses the cells own biosynthetic machinery to produce proteins encoded by viral genes (Wagner et al, 2004). Viral proteins are broken down into peptides by enzymes within the cell (proteasomes) (DeFranco et al, 2007). Following this, the peptides are carried into the endoplasmic reticulum by a TAP transporter (Sompayrac, 2003). After which MHC class I molecules within the cell are loaded with these peptides along with a sample of other normal proteins

being made by the cell. This MHC-peptide complex is then transported to the cell surface for presentation. The protein fragments are displayed on MHC class I molecules to cytotoxic T cells (Tc) (Schindler, 1991). Having this mechanism in place allows all body cells to be monitored by CD8+ve Tc cells which inspect the cells. Tc cells detect foreign peptides bound to an MHC so if a cell has been invaded by a virus or parasite, the Tc cells are alerted and respond by destroying the abnormal cell thus preventing the spread of viruses throughout the body (DeFranco et al, 2007).

MHC class II molecules are designed to present peptides to helper T cells (Th). Unlike the MHC class I molecules, MHC class II molecules are restricted to certain cell types termed professional APC’s. Their focus is on events unfolding in the outside environment so can present samples of antigens derived from exogenous antigens in various parts of the body. Professional APCs display class I and class II MHCs as well as co-stimulatory signals (Sompayrac, 2003). In order to function, T cells, both Tc and Th cells, require activation. For this to happen, T cells need to recognise its cognate antibody in an MHC complex and they also need a co-stimulatory signal which can only be provided by professional APCs (Wellness. com, 2010). Co-stimulation is provided by a protein (B7) on APCs which interlocks with another protein (CD28) on the surface of T cells.

Examples of professional APCs are activated macrophages, activated dendritic cells (DC) and activated B cells. DCs are the most important of the APCs as it capable of initiating an immune response by activating naïve T cells (Sompayrac, 2003). These cells are strategically located in areas of the body such as the skin, mucosal lining of lung and digestive tract where

microbes are likely to enter (Sherwood et al, 2009). In normal tissues DCs are immature, expressing few B7 protein and MHC molecules on their surfaces so are poor antigen presenters. However, when a microbe(s) invade the tissue which DCs reside, they mature. DC are specialised as they have pattern recognition receptors on their surface which recognises common features of invading microbes such as LPS on the surface of gram negative bacteria. DCs takes up pathogens through receptor mediated endocytosis and degrade it in a lysosome (DeFranco et al, 2007). During a invasion, cytokines (TNF α) released by activated macrophages are recognised by the DC which informs it that innate immune system is ‘ under attack’. Cytokines bind to receptors on the DC causing it to cease phagocytosis, leave the tissues (site of infection) and migrate through the lymphatic system. Whilst travelling, the DC equips the class II MHC reserves with the antigen and also produces B7 co-stimulatory protein. During this time also, DC upregulates the expression of class I MHC molecules as a precautionary measure that if the DC was infected by a virus or parasite at the site of infection, the antigen could be processed into protein fragments for presentation if necessary (Male, 2004). By the time the DC reaches the lymph node, it has its co-stimulatory molecules and the MHC class II- peptide complex(es) primed and ready to activate naïve T cells.

Lymph nodes have compartments that have bountiful supplies of B and T cells (Schindler, 1991). Whilst at the lymph node, DCs trigger the adaptive immune response by presenting antigens to CD4+ve Th cells with matching receptors (Sherwood, 2009). After which, the APC secrete interleukin, a chemical which activate Th cells. Activated Th cells then secretes cytokines

which stimulates the Th into rapid proliferation and differentiation into effector Th cells and memory Th cells (DeFranco et al, 2007). Memory Th cells are useful in future infections by the same pathogen whilst effector Th cells activate B cells to secrete antibodies enhancing other immune activities (Sherwood, 2009). Additionally effector Th cells and antibody molecules depart from the lymph node and enter the circulation which they then leave at the infection site. Antibodies opsonise the bacteria enhancing their uptakes by phagocytes, stimulate Natural killer cells (NK) to directly lyse the bacteria and also activate the lethal compliment system (Sherwood, 2009). CD4 +ve T-cell on the other hand activate macrophages to become more cytotoxic.

‘ It is important that the magnitude of the immune response be in proportion to the seriousness of the attack’ (Sompayrac, 2003). As previously mentioned DCs migrate to lymph nodes only when activated by ‘ battle’ cytokines. In a serious infection, many cytokines are released and thus more DCs are activated. Before their migration to lymph nodes, activated DCs release chemokines, a chemical which triggers precursor cells (monocytes) to leave the blood stream and become their replacement as DCs in (Sompayrac, 2003). These new DCs are then able to be activated and make their way to the lymph node which amplifies the response to the invasion. The new recruits of DC’s are like ‘ photojournalists’, the antigenic peptide which they carry to the lymph node being a ‘ snapshot’ of the infection site (Sompayrac, 2003). This is useful so if there are changes in the area, the appropriate T cell can be activated and thus elicit the immune response most suitable. If the infection is mild, there will be fewer cytokines produced,

less DCs activated, fewer chemokines released, fewer replacements of DCs therefore the number of DCs that make their way to the lymph node will also be significantly less. Consequently the number of B and T cells that becomes activated in the lymph nodes relies greatly on the number of DCs present.

As detailed above DCs play a role in the activation of macrophages. Macrophages are one of the early defences against invaders that initiate the cell mediated immune response (Schindler, 1991). Macrophages are very weak at presenting antigens as they only possess enough MHC molecules and co-stimulatory proteins when activated by ‘ battle’ cytokines e. g. IFN γ (DeFranco et al, 2007). Macrophages function in the re-stimulation of experienced T cells so they continue to partake in the fight against the pathogen (Male, 2004). They engulf pathogens that have invaded the tissues, process it using internal enzymes and present the peptides on MHC class II molecules. This continual display of antigens is recognised by Th cells which continue to complete their function. Next the activated macrophage releases cytokines are previously mention that act on the DC i. e. TNF α. Other cytokines released includes IL-1 and IL-8. IL-1 aids in the activation of B and T cells (Schindler, 1991).

B cells are the third professional APC. At the start of an infection B cells are naïve so do not play a definitive role. However throughout the course of the infection B cells become activated. Some B-cells are specific to T-independent antigen so only require binding of its receptor (BCR) to a cognate antigen for activation (Sherwood 2009). Other B-cells are specific to T-dependent antigen so after processing the antigen and displaying it on MHC class II molecules, binding of a Th cell is required for their activation.

The MHC class II complex interacts with the TCR on the CD4+ Th cell which recognise the specific antigen on the B cell. Next the helpers release a chemical known as interleukin triggering the activation of the B cell. Activated B cells go through rapid proliferation and differentiation into memory cells and antibody producing plasma cells (Sherwood, 2009). B cells have the advantage of presenting the antigen very quickly so makes the immune response more efficient.

The development of two different pathways of antigen presentation i. e. via MHC class I and II molecules can be rationalised in that each ultimately helps to elicit the most appropriate immune response through stimulation of the T cell the population most effective in eliminating the pathogen in question.

MHC class I APCs allows for the monitoring of all body cells through Tc cells whilst MHC class II APCs seek the help of Th cells and B cells which directs the immune response in a way that corresponds to the seriousness an infection. Through these functions, APCs ultimately helps to maintain health and life.