Compare and contrast the development of b and t cells

The epithelial surfaces of the body serve as an effective barrier against most microorganisms, and they are rapidly repaired if wounded. Adaptive immunity is initiated when an innate immune response fails to eliminate a new infection, whereby an activated antigen presenting cells (APCs) bearing pathogen’s antigens are delivered to the draining lymphoid tissues. An adaptive immune response differs from the innate immunity in its ability to target structures that are specific to particular strains and variants of pathogen.

T cells are produced in the bone marrow. They are transported still, as pro-thymocytes to the thymus where they undergo the process of maturation and selection. The regulation of T cell maturation in the thymus is termed ‘ central tolerance’. During gestation, most T cells generated bear the gamma/deta T cell receptor (TcR) on their surface. In the adult, most T cells bear the alpha/beta TcR. The newly formed TcR then, has to be tested for recognition of self-MHC/peptide. The T cells are tested at a stage of development known as double positive, meaning that they bear both CD4 and CD8 receptors on their surface. Cells with TcRs that recognize self-MHC/peptide with very low affinity will die. This process is known as death by neglect. Cells with TcRs with medium affinity for MHC receive survival signals and undergo a process known as positive selection. Finally, cells which receive a high affinity signal via their TcR die by apoptosis, a process known as negative selection. Cells that interact with MHC class I become CD8 positive T cell, and those that interact with MHC class II become CD4 positive T cells, before migrating out into the peripheral lymphoid system (Wood P, 2006).

Mature B cells, like T cell, are also develop form pluripotent stem cells. However unlike T cells lymphocytes, B cell maturation occurs in the bone marrow. There are four different stages of B cell development: pro-B, pre-B, immature B, and mature B cells. During its development, B cells acquire B cell surface marker expression such as B220, CD19, CD20, etc. as well as antigen receptors. The stromal cells lining the bone marrow provide essential growth signals to developing B cells, including cytokines such as IL7 and cell to cell contact, via VLA4/VCAM and Kit/SCF. During B cell development, gene segment rearrangements take place, just like in T cells where TcR rearrangements (central tolerance) also occur. However, for B cells, the immunoglobulin heavy chain gene locus (variable-V, joining-J and diversity-D segments), situated on chromosome 14, rearranges. In haematopoietic stem cells, the Ig heavy chain genes are in germline configuration (Kurosaki T et al., 2009). As B cells develop to pro-B cells, a D-J recombination is the first gene rearrangement to take place. The intervening DNA is normally deleted from the chromosome as a circle. Gene rearrangements are mediated by recombinase activitng genes, RAG proteins. As the developing B cell proceeds from pro- to pre-B cell stage, a V-DJ gene arrangement takes place to form the VDJ coding block that encodes the variable domain on the antibody heavy chain. Gene rearrangement takes place on both copies of chromosome 14 in a developing B cell, but once a productive VDJ block has been assembled on one chromosome 14, rearrangement ceases on the other chromosome, ensuring only one type of Ig is produced by any single B cell. This process is known as allelic exclusion. If a developing B cell fails to make a productive VDJ block, it will fail to produce antibody heavy chain and die in the bone marrow (Murphy K et al, 2008).

T and B cell activation:

T cell activation takes place in draining lymph nodes (also spleen) close to site of infection. T cell recognizes antigen on MHC (Major Histocompatibility Complex) molecules becomes activated and differentiates to effector cells. Effector T cells migrate to site of infection and carry out effector functions. The T lymphocytes arrive through venules, and cross through the endothelial to the lymph nodes. Antigen presenting cells such (APC) such as dendritic cells, and macrophages presented antigens to T cells. On recognition of the antigen, a low affinity interaction is formed. These T cells then leave lymph node though the lymphatic system. Those T cells that recognize the antigen's wall with high affinity will be retained and the process of proliferation and differentiation occurs. However, initial B cell activation takes place in T cell zone of secondary lymphatic tissues (i. e. in lyhmph nodes). Mostly IgM producing plasma cells are produced at this state. B cells, unlike T cells, are activated by the ineraction with antigen-specific T cell, by linked recognition. Antigen-activated B cell migrates to B cell area of lymph nodes to form organized germinal centres, where additional B cell differentiation processes take place. It is important to note that T cells recognize the peptide, while B cells recognize the coat protein.

For T and B lymphocyte activation 2 signals are hypothesized to be required. Firstly, the antigen stimulus signal and secondly, the co-stimulatory stimulus. The absence of the second signal results in anergy or apoptosis. CD28/B7 interaction is the co-stimulatory signals for T cells while CD40/CD40 ligand, on the activated T cells, interaction is for B cells. For both T and B lymphocytes, in it resting G0 cell cycle, the cell appear to have a large

nucleus, with little cytoplasm and show little evidence of organelles. However, when these cells enter G1/S/G2 cell cycle, cell shows an increase in cell size, chromatin de-condensation is seen. Cell division occurs rapidly, generating effector cells of either T or B lymphocytes. Effector T cells include Th1, Th2 and T regulatory, as well as T cytotoxic cell and memory T cells. On the other hand, effector B cells include plasma cell and memory B cell.

T and B cell effector functions:

B cell response to T-dependent protein antigen results in germinal centres formation in B cell areas of lymph nodes, and specialized processes such as Ig class-switching, somatic mutation and affinity maturation, memory B cell and plasma cell generation take place there. Emerging form germinal centres are somatically mutated and class-switched B cells, which no longer just produce IgM. Memory B cells are long-lived, resting and re-circulating cells, responsible for immunization part which helpto generate rapid and vigorous immune response on second encounter for that specific antigen. Plamablast cells migrate to other sites such as bone marrow, and become plasma cells, producing large amounts of secreted antibody. Some of which can live for long periods. The effector functions of B cells refer to what antibodies do after their contact with the antigen. The antibody effector functions include neutralization, complement fixation (IgM, IgG1/2/3), oposonization and antibody dependent cell-mediated cytotoxicity.

In contrast, T cell effector functions differ significantly from B cell effector functions. Antigen presenting cells present peptide via MHC which can either interact with CD4+ or CD8+ T cells. Helper T cells are defined by the cytokines they produce. Naïve CD4+ T cells (Th0), on interaction with APC,

can differentiate to Th1 or Th2 cells, depending on the cytokine environment. Th1 cells co-ordinate inflammatory immune responses to intracellular pathogens while Th2 cells help B cells to make antibodies required for immune responses to extracellular pathogens, this is known as humoral immunity. Th1 and Th2 cells both act to promote the generation of more leukocytes. Besides Th0/Th1/Th2, other CD4+ T cell subsets exist (Zhu J et al., 2010). Resting T cells can differentiate into activated helper T cell, as well as activated cytotoxic T cell (CD8+ T cell). Initially, CD8+ T cells interact with potential target cells via low affinity/non-specific interactions between adhesion molecules on the T cell (LFA-1 and CD2) and the target cell (ICAM1, ICAM2). This interaction has no effect on the cytoskeleton of the T cell and is a transient interaction unless recognition of specific peptide: MHC complexes occurs. If peptide: MHC I complex is present, the affinity of the adhesion molecule interaction increases and there is clustering of T cell receptor and associated molecules at the point of contact with the target cell forming the immunological synapse. This also signals for cytoskeletal rearrangements organized by the microtubule organizing complex which focuses the cytotoxic granules of the T cell at the point of contact with the target. Notice here, that T cells, unlike B cells do not produce antibodies against antigens. Granules containing perforin and other enzymes including granzymes are released and induce the activation of the cathepsin pathways in the target cell leading to apoptosis. CD8+ T cells can also kill target cells via the Fas/FasL pathway which also induces apoptosis (Peter EJ 2007).

In conclusion, adaptive immune responses occur when individual lymphocytes capable of responding to antigen proliferate and differentiate to

become an antigen-specific effector cells and memory cells. The process of lymphocyte cell cycle progression, proliferation and differentiation in response to antigen and stimuli is known as lymphocyte activation. B cell activation is initiated by the ligation of the B cell receptor (BCR) with antigen and ultimately results in the production of protective antibodies against potentially pathogenic invaders. While naive or memory T cells encounter foreign antigen along with proper co-stimulation they undergo rapid and extensive clonal expansion. In human, this type of proliferation is fairly unique to cells of the adaptive immune system and requires a considerable expenditure of energy and cellular resources.