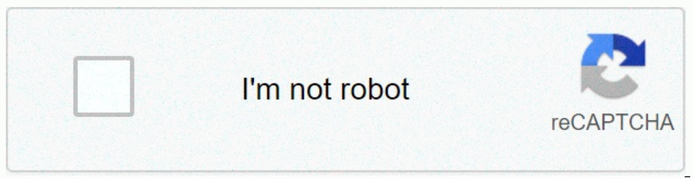

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How b cells recognize and respond to an antigen

Learning objectiveS Describe B cell production and maturation Compare B-cell receptor and T-cell receptor structure Compare T-dependent and T-independent B cell activation Compare primary and secondary antibody responses Humoral immunity refers to adaptive immune mechanisms mediated by antibodies emitted by B lymphocytes or B cells. This section will focus on B cells and discuss their production and maturation, receptors and activation mechanisms. B Cell production and maturation Like T cells, B cells are formed from multi-stage hematopoietic stem cells (HSCs) in the bone marrow and follow the pathway through lymphoid stem cells and lymphoblasts (see Figure 1 Cellular Defenses). Unlike T cells, however, lymphoblasts designed to become B cells do not leave the bone marrow and go to the thymus gland for maturation. Rather, perhaps B cells continue to mature in the bone marrow. The first step in b cell maturation is to estimate the functionality of their antigen binding receptors. This occurs by using positive selection of B cells with normal functional receptors. A negative selection mechanism is then used to prevent self-reactive B cells and reduce the risk of autoimmunity. Negative selection of self-reactive B cells may include elimination by apoptozy, receptor editing or modification so that they are no longer self-reactive, or an anergy induction into cell B. Immature B cells that pass the selection of bone marrow, then proceed to the spleen in their final stages of maturation. There they become previously untreated mature B elements, i.e. mature B cells that have not yet been activated. Think about this Compare maturation of B cells to maturation of T cells. Figure 1: B cell receptors are embedded in b cell membranes. The variable regions of all receptors in the same cell bind the same specific antigen. Like T cells, B cells have antigen-specific receptors with different characteristics. Although they use T cells for optimal function, B cells can be activated without the help of T cells. B cell receptors (BcRs) in previously untreated, mature B cells are membrane-related forms of IgD and IgM monomer. They have two identical heavy chains and two identical light chains connected to disulphide bonds in the basic Y form (Figure 1). The stem of a Y-shaped molecule, a permanent region of two heavy chains, covers the B-cell membrane. Both antigen binding sites exposed to the outside of cell B are involved in the binding of specific pathogen epitopes to initiate the activation process. It is estimated that each previously untreated mature B cell has more than 100,000 BKR on its membrane, each of which has the same epitopal binding specificity. In order to be able to prepare to respond to a wide range of microbial epitopes, B cells, such as T cells, use genetic large segments of genes to ensure the diversity of the required receptor specificity. The BCR heavy chain variable region consists of segments V, D and J, similar to β TCR variable chain. The variable region of the BCR light circuit consists of V and J segments, α the TCR variable chain. The genetic reordulation of all possible combinations of V-J-D (heavy chain) and V-J (light chain) provides millions of unique antigen binding sites for BCR and antibodies released after activation. One important difference between BcRs and TKR is the way they can interact with antigenic epitopes. Whereas TCR can only interact with antigen epitopes presented in the MHC I or MHC II antigen binding cleft, BKR does not require the production of antigen by THE MHC; they may interact with epitopes on free antigens or epitopes visible on the surface of intact pathogens. Another important difference is that TKR only recognises protein epitops, while BKR can recognize epitops associated with different molecular classes (e.g. proteins, polysaccharides, lipopolisaccharides). B cell activation occurs using different mechanisms depending on the molecular class of the antigen. For the activation of b cells with protein antigen B cell should act as APC, showing protein epitops with MHC II to help T cells. Due to their dependence on T cells for B cell activation, protein antigens are classified as T-dependent antigens. In contrast, polysaccharides, lipopolisaccharides and other non-protein antigens are considered T-independent antigens because they can activate B cells without antigen treatment and presentation to T cells. Think about what types of molecules serve as BCR? What are the differences between TKR and BKR in antigen recognition? Which classes of molecules are T-dependent antigens and what are T-independent antigens? B cell activation without the help of T-cell collaboration is called T cell independent activation and occurs when BKR interacts with T-independent antigens. T-independent antigens (e.g. polysaccharide capsules, lipopolysaccharide) are repetitive epitope units in their structure, and this repetition allows multiple BKR interlinking, providing the first signal for activation (Figure 2). Since T cells are not involved, the second signal should come from other sources, such as charging receptor interactions with PAMPs or interactions with complement system factors. When cell B is activated, it is proliferated and the daughter cells differ in plasma cells. Plasma cells are antibody factories that emit large amounts of antibodies. After differentiation, the surface BKR disappears and the plasma cell releases pentameric IgM molecules that have the same antigen (Figure 2). T-cell-independent reaction is temporary and does not lead to the formation of memory B cells. Thus, it will not send a secondary response to future exposure to T-independent antigens. Figure 2: In the first T independent antigens have reusable epitopes that can cause B cell recognition and activation without the help of T elements. A second signal is also required to activate the B cell, such as ttl interaction with PARP (not shown). When activated, B cell proliferates and atheus antibody secretion plasma cells. Think about this What are the two signals needed to independent activate T-cells in B cells? What is the function of a plasma cell? Figure 3: Click for a larger picture. The activation of cells B dependent on T-cell B cells in cells B recognises and internalises the antigen and offers it to the helper T for the cell specific to the same antigen. The helper T cell interacts with the antigen provided by cell B, which activates the T cell and stimulates the release of cytokines, which then activates the B cell. Activation of cell B causes proliferation and differentiation in B cells and plasma cells. T-cell-dependent B cell activation is more complex than independent activation of T cells, but as a result, the immune response is stronger and develops memory. T-cell-dependent activation may occur either in response to free protein antigens or to protein antigens associated with an intact pathogen. The interaction between BKR on a previously untreated mature B cell and the free protein antigen stimulates the internalisation of the antigen, while interactions with antigens associated with intact pathogens initiate antigen extraction from the pathogen before internalization. After the internal protein inside cell B, the protein antigen is processed and presented with MHC II. The submitted antigen is then recognized by the helper of T cells specific to the same antigen. The TCR of the assistant T cells recognizes foreign antigen, and the T cell CD4 molecule interacts with MHC II on the B cell. Coordination between B cells and helper T cells specific to the same antigen is called related recognition. When activated by related recognition, TH2 cells produce and secrete cytokines that activate b cells and cause proliferation of clone in daughter cells. After several rounds of proliferation, additional cytokines provided by TH2 cells stimulate the differentiation of activated B cell clones in memory B cells, which will react rapidly to further exposure to the same protein epitope and plasma cells that lose membrane BKR and initially release pentameric IgM (Figure 3). Following the initial secretion of IgM, cytokines released by TH2 cells stimulate plasma cells to move from IgM production to IgG, IgA or IgE. This process, called class switching or switching allows plasma cells that are cloned from the same activated B cells to produce different classes of antibodies with the same epitope specificity. Class switching is performed by genetic rearrangement of gene segments that encode a permanent region that determines the antibody class. The variable region remains unaldid, so the new antibody

class retains the specificity of the original epitopes. Think about what steps are needed to activate T-cell dependent b cells? What is antibody class switching and why is it important? T-cell-dependent B cell activation plays an important role in both primary and secondary reactions associated with adaptive immunity. The first use of protein antigen results in a T-cell-dependent primary antibody response. The initial phase of the primary response is approximately a 10-day shift period or a latent period during which antibodies cannot be detected in serum. This delay period is the time required for all stages of the primary response, including previously untreated, mature binding of Antigen B cells to Erces, antigen treatment and presentation, assistive T cell activation, B cell activation and clonal proliferation. The end of the shift period is characterized by an increase in IgM levels in serum, as TH2 cells stimulate b cell differentiation in plasma cells. IgM levels peak at about 14 days after exposure to the primary antigen; th2 stimulates antibody class ossion at approximately the same time, and serum IgM levels begin to decrease. At the same time, IgG levels rise until it reaches a maximum of approximately three weeks in the primary response (Figure 4). During the primary response, some cloned B cells are differentiated into memory B cells programmed to respond to future exposures. This secondary response occurs faster and more strongly than the primary response. The delay period is reduced to only a few days and IgG production is significantly higher than the primary response (Figure 4). In addition, antibodies obtained during secondary response are more effective and associate with greater affinity with target epitopes. Plasma cells produced during secondary responses live longer than during the primary response, so the levels of specific antibodies remain elevated for a longer period of time. Figure 4: Secondary antibody responses occur more quickly compared to the primary response and produce higher and longer-lasting antibody levels. Secondary responses include IgG. Think about what events occur during the delay period of primary antibody response? Why do antibody levels remain elevated for longer during secondary antibody response? The main concepts and summary of B lymphocytes or B cells produce antibodies involved in humoral immunity. B cells are produced in the bone marrow, where maturation stages, stages, go to the spleen to obtain the last stages of maturation in previously untreated mature B cells. B-cell receptors (BcR) are membrane-related forms of IgD and IgM monomers that bind specific epitops of the antigen to their Fab antigen-binding regions. The diversity of the binding specificity of antigen is due to the genetic reorlagation of the V, D and J segments, which are similar to the mechanism of TCR diversity. Protein antigens are called T-dependent antigens because they can only activate B cells in collaboration with the helper's T cells. Other molecule classes do not require T-cell collaboration, and are called T-independent antigens. T-cell independent B cell activation includes the binding of BKRsu to recurrent nonprotein antigen epitopes. It is characterized by the production of IgM by plasma cells and does not produce memory B cells. T-cell-dependent B cell activation includes the processing and presentation of protein antigens in the help of T cells, the activation of B cells with cytokines released from activated TH2 cells, and plasma cells that produce different classes of antibodies caused by a change in therapy. Memory B cells are also produced. Secondary effects on the T-dependent antigen cause a secondary antibody reaction caused by memory B cells. The secondary response develops more rapidly and produces higher and longer-lasting levels of antibodies with a higher affinity for the antigen in question. Which of these would be a T-dependent antigen? lipopolisaccharide glikolipid protein carbohydrates Which of these should be BCR? Which of these does not occur during the delay period of primary antibody responses? Activation of the helper T cell class switching to the IgG presentation antigen with MHC II binds antigen to BCRs _____ antigens can stimulate B cells to activate, but require cytokine help provided by helper T cells. T-independent antigens can stimulate B cells to activate and secrete antibodies without the help of helper T cells. These antigens have _____ antigen epitopes that cross the link to BKR. The patient lacks the ability to perform a functioning T cell due to genetic disorders. Could these patients' B cells produce antibodies in response to infection? Explain your answer. Answer.

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