B cell activation and differentiation I

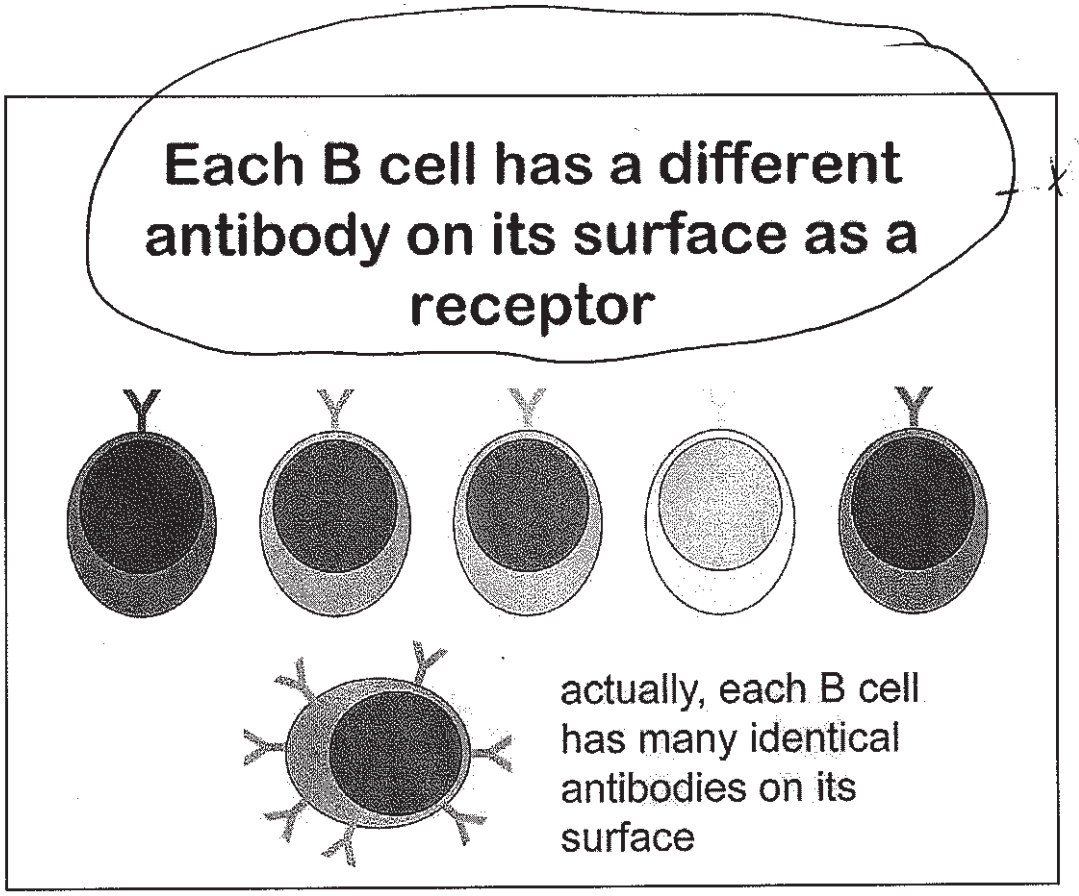
Parham, 3rd ed
Ch. 9, 9.1-9.6; Ch. 4, 4.10-4.13

Name - course - year

The goal of this lecture is to learn about B cell activation and differentiation. The lecture will cover the B cell surface receptors involved in activating a B cell, and the different B cell functions resulting from B cell activation.

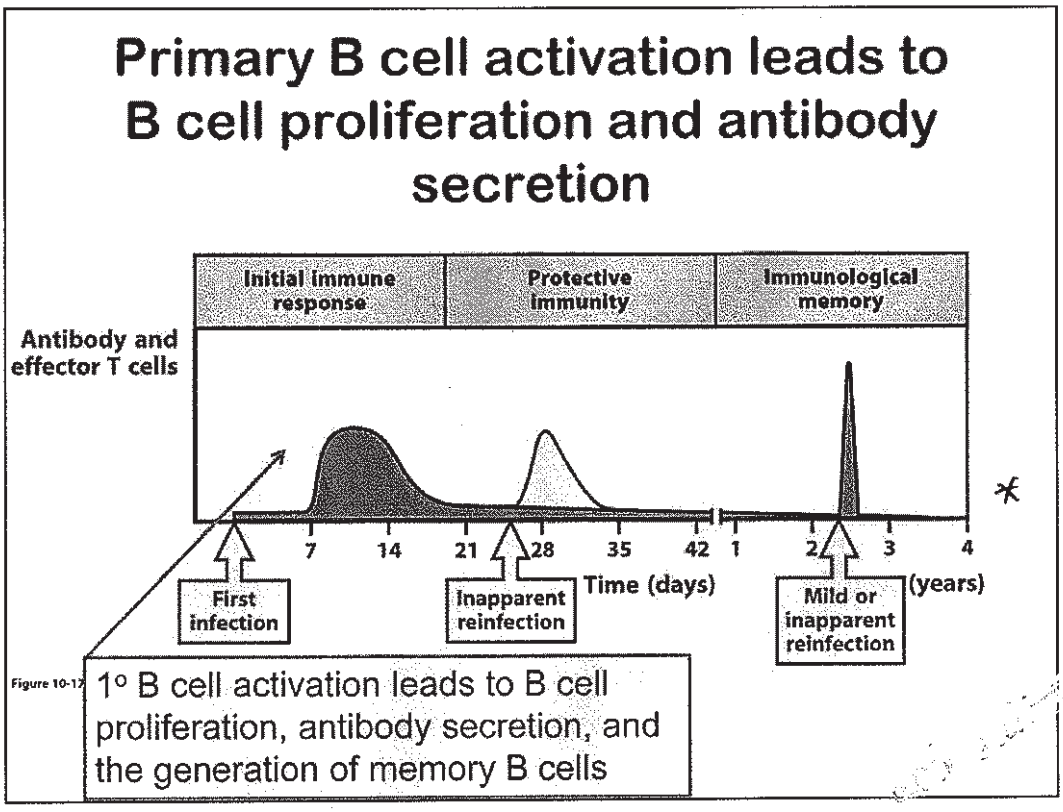
Learning Objectives

- Describe the B cell receptor signaling complex and the role of complement in enhancing B cell activation
- Name the difference between T cell-dependent and T cell-independent B cell activation
- Outline the molecular mechanism by which a B cell produces secreted versus membrane-bound forms of the antibody
- Describe the role of lymph nodes in B cell responses
- List the major events that occur in a germinal center



Title summarizes key points

Each B lymphocyte has a different antibody on its surface as a receptor. In fact, each B lymphocyte actually has many tens of thousands of copies of the same antibody on its surface, but these antibodies are different from the antibodies on each other B cell.



*note: citation is included in course materials. Should be on slide as well.

Well-labeled graphics

One of the hallmarks of the adaptive immune response is its ability to improve upon re-exposure to the same pathogen. This is often referred to as immunological 'memory'. When an individual first encounters a pathogen, the initial response (called the primary or 1° response) has a long lag time before it is detectable, usually on the order of one week. This response then improves over the following week, and then declines, leaving a residual level of antibodies and T cells that provide protective immunity. This protective immunity can last for years or even for the lifetime of the individual, and if the individual is reinfected with the same pathogen there is little sign of disease. Upon re-infection, the adaptive immune response is re-activated. This second time around (referred to as secondary or 2° exposure), the T cell and antibody responses occur much faster than in the primary response, they are of higher magnitude, and therefore, they are more effective at clearing the pathogen.

Since antibodies are produced by B cells, we can examine the mechanism underlying the improved response upon secondary exposure by studying the changes in B cells following the first infection and then the reinfection. One important aspect of this process is that following the primary infection, B cells are activated and proliferate. Some of these cells become antibody-secreting cells and others become memory B cells. Memory B cells can be reactivated upon secondary exposure, and will rapidly divide to produce large numbers of antibody-secreting cells.

Summary of key points

- **Membrane-bound IgM is in a complex with invariant chains called Igα and Igβ, forming the BCR**
- **Igα and Igβ each contain an ITAM motif**
- **B cells express a co-receptor composed of CD21, CD18, and CD81 that binds complement, increasing B cell signaling**
- **BCR aggregation, either alone or together with the co-receptor, is the stimulus that leads to the activation of downstream signaling pathways**
- **Transcription factors are activated leading to new gene expression that induces B cell proliferation and differentiation**

inserted periodically

Mix of text and graphic slides

Summary of key points.

1. Membrane-bound IgM is in a complex with invariant proteins chains called Ig-alpha and Ig-beta, forming the BCR.
2. Ig-alpha and Ig-beta each contain an ITAM motif.
3. B cells express a co-receptor composed of CD21, CD18, and CD81 that binds to complement, increasing B cell signaling.
4. BCR aggregation, either alone or together with the co-receptor, is the stimulus that leads to activation of downstream signaling pathways.
5. Transcription factors are activated leading to new gene expression that induces B cell proliferation and differentiation.

How do naïve lymphocytes and antigen find each other?

- **Naïve B cells recirculate through secondary lymphoid organs**
  - **Naïve B cells have homing receptors that direct them to enter lymph nodes**
- **Lymph nodes collect pathogens and antigens from all tissues in the body via the lymphatics**

Pause for question slides

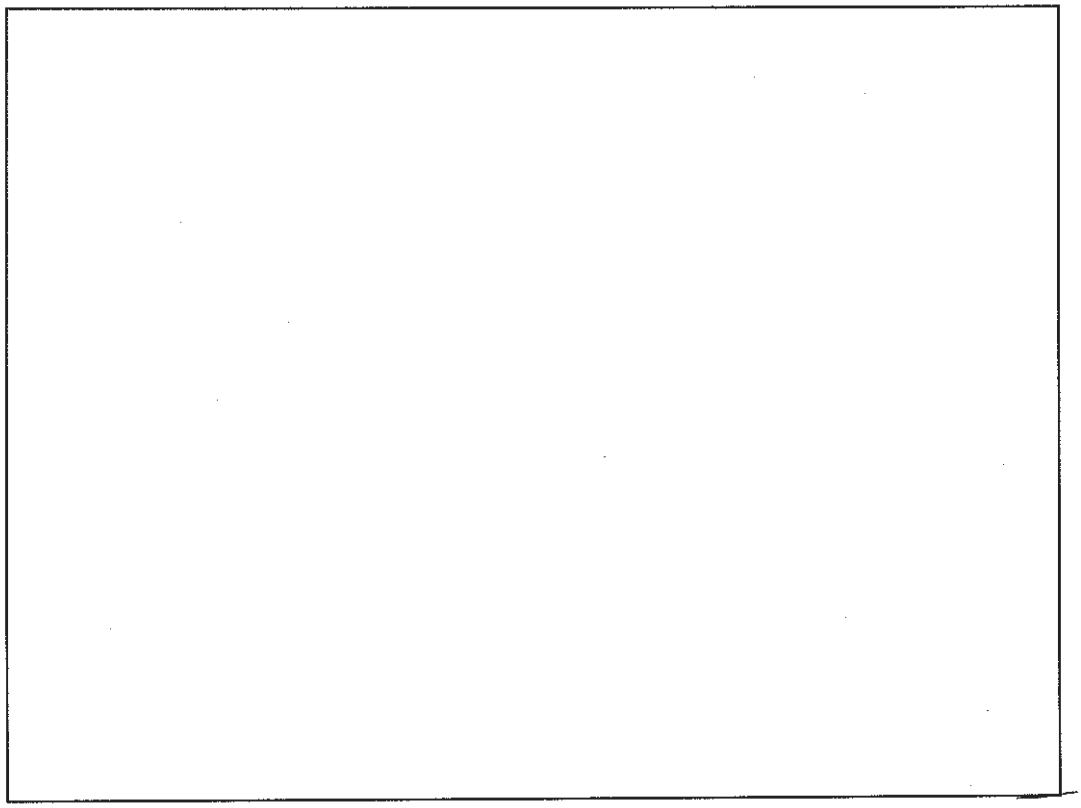
Can use audience response system, open discussion or quiet student consideration

In order for a naïve B cell to be activated during an infection, the pathogen and the B cell need to come together. In addition, in the case of T cell-dependent B cell activation, a helper CD4+ T cell also needs to be present. These interactions take place in secondary lymphoid organs, such as the lymph nodes and spleen.

As you learned last year in immuno-histology, naïve B cells are recirculating cells that traffic from the blood through secondary lymphoid organs and then back to the blood, and so on. In this way, each B cell can check out each secondary lymphoid organ in the body roughly once a day. From the blood, naïve B cells are directed to enter lymph nodes by their expression of homing receptors and chemokine receptors.

In addition, lymph nodes collect pathogens and antigens from all tissues in the blood via the lymphatics.

If the infection is in the blood, the pathogen will be trapped in the spleen. B cells in the blood also traffic through the spleen.



Study Questions

1. What triggers B cells to proliferate and become antibody-secreting cells?
2. What is different about a secondary antibody response compared to the primary response?
3. How does the BCR signal?
4. What are Igα and Igβ? What is an ITAM?
5. What is the major B cell co-receptor?
6. What is a T cell-dependent compared to a T cell-independent antibody response?
7. How do B cells go from expressing their antibody protein as a surface receptor to a secreted protein?
8. Where do B cells first get activated?
9. What is a germinal center?