13.2C: Antibody-dependent Cellular Cytotoxicity (ADCC) by Natural Killer Cells

Skills to Develop

1. **Discuss** how antibodies defend the body by way of **ADCC by Natural Killer cells**. (Include what classes or isotypes of immunoglobulins are involved, the role of the Fab portion of the antibody, the role, if any, of the Fc portion of the antibody, and the role of any complement proteins, if any, involved.)

Natural killer (NK) cells are capable of antibody-dependent cellular cytotoxicity or ADCC. NK cells have receptors on their surface for the Fc portion of certain subclasses of IgG. When the antibody IgG is made against epitopes on "foreign" membrane-bound cells, such as virus-infected cells and cancer cells, the Fab portions of the antibodies react with the "foreign" cell. The NK cells then bind to the Fc portion of the antibody (Figure 13.2.1).

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https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_6%3A_Adaptive_Immunity/13%3A3A...
Figure 13.2.1: Destruction of Virus-Infected Cells by NK Cells through Antibody-Dependent Cellular Cytotoxicity (ADCC), (left) Step 1: The Fab portion of the antibody binds to epitopes on the "foreign" cell. The NK cell then binds to the Fc portion of the antibody. (right) Step 2: The NK cell is then able to contact the cell and release pore-forming proteins called perforins and proteolytic enzymes called granzymes. Granzymes pass through the pores and activate the enzymes that lead to apoptosis of the infected cell by means of destruction of its structural cytoskeleton proteins and by chromosomal degradation. As a result, the cell breaks into fragments that are subsequently removed by phagocytes.

Perforins can also sometimes result in cell lysis.

The NK cell then releases pore-forming proteins called perforins, proteolytic enzymes called granzymes, and chemokines. Granzymes pass through the pores and activate the enzymes that lead to apoptosis of the infected cell by means of destruction of its structural cytoskeleton proteins and by chromosomal degradation (Figure 13.5.1; right panel and Figure 12.5.2). As a result, the cell breaks into fragments that are subsequently removed by phagocytes. Perforins can also sometimes result in cell lysis. (When NK cells are carrying out ADCC, they are sometimes also referred to as killer cells.)
**Figure 13.2.2:** NK cells release pore-forming proteins called perforins and proteolytic enzymes called granzymes. Granzymes pass through the pores and activate the enzymes that lead to apoptosis, a programmed suicide of the infected cell. Apoptosis occurs when certain granzymes activate a group of protease enzymes called caspases that destroy the protein structural scaffolding of the cell, degrade the cell's nucleoprotein, and activate enzymes that degrade the cell's DNA. As a result, the infected cell breaks into membrane-bound fragments that are subsequently removed by phagocytes. If very large numbers of perforins are inserted into the plasma membrane of the infected cell, this can result in a weakening of the membrane and lead to cell lysis rather than apoptosis. An advantage to killing infected cells by apoptosis is that the cell's contents, including viable virus particles and mediators of inflammation, are not released as they are during cell lysis.

Video: YouTube animation illustrating the detailed cellular mechanism behind apoptosis. [https://www.youtube.com/watch?v=9KTDz-ZisZ0](https://www.youtube.com/watch?v=9KTDz-ZisZ0)

Exercise: Think-Pair-Share Questions

Explain how IgG can work with NK cells to kill virus-infected cells.

**Outside Links**

1. Flash animation of ADCC contact by NK cells.
2. html5 version of animation for iPad showing ADCC contact by NK cells
3. Flash animation of apoptosis by NK cells.
4. html5 version of animation for iPad showing apoptosis by NK cells.
Summary

NK cells are capable of antibody-dependent cellular cytotoxicity or ADCC. When IgG is made against epitopes on "foreign" membrane-bound cells, such as virus-infected cells and cancer cells, the Fab portions of the antibodies react with epitopes on the "foreign" cell and then NK cells bind to the Fc portion of the antibody. The NK cell then releases pore-forming proteins called perforins and proteolytic enzymes called granzymes. Granzymes pass through the pores and activate the enzymes that lead to apoptosis of the infected cell and the cell breaks into fragments that are subsequently removed by phagocytes.

Questions

Study the material in this section and then write out the answers to these questions. Do not just click on the answers and write them out. This will not test your understanding of this tutorial.

1. Discuss how antibodies defend the body by way of ADCC by NK cells. (Include what classes or isotypes of immunoglobulins are involved, the role of the Fab portion of the antibody, the role, if any, of the Fc portion of the antibody, and the role of any complement proteins, if any, involved.)

2. Antibody-dependent cellular cytotoxicity (ADCC) is a result of:
   a. Antibodies sticking infected cells and cancer cells to phagocytes.
   b. Antibodies sticking infected cells and cancer cells to cytotoxic T-lymphocytes (CTLs).
   c. Antibodies sticking infected cells and cancer cells to NK cells.
   d. MAC lysing the membranes of infected cells and cancer cells.

3. During ADCC, the Fab portion of the antibody ___________while the Fc portion _______________.
   a. binds to epitopes of an antigen; activates the complement pathway.
   b. activates the complement pathway; binds to epitopes of an antigen.
   c. binds to epitopes of an antigen; binds to cytotoxic T-lymphocytes.
   d. binds to epitopes of an antigen; binds to NK cells.

4. NK cells kill the cells they bind to by:
   a. Triggering apoptosis.
   b. Dumping the contents of their lysosomes on the cell.
   c. Producing cytolytic exotoxins that lyse the cell.
   d. Inducing extracellular killing by eosinophils.

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