LEARNING OBJECTIVE

- Describe the role of natural killer cells in the immune response

Lymphocytes are leukocytes (white blood cells) that are histologically identifiable by their large, darkly-staining nuclei; they are small cells with very little cytoplasm. After a pathogen enters the body, infected cells are identified and destroyed by natural killer (NK) cells, which are a type of lymphocyte that can kill cells infected with viruses or tumor cells (abnormal cells that uncontrollably divide and invade other tissue). While NK cells are part of the innate immune response, they are best understood relative to their counterparts in the adaptive immune response, T cells, which are also classified as lymphocytes.

T cells are lymphocytes that mature in the thymus gland and identify intracellular infections, especially from viruses, by the altered expression of major histocompatibility class (MHC) I molecules on the surface of infected cells. MHC I molecules are proteins on the surfaces of all nucleated cells which help the immune system distinguish between "self" and "non-self." If the cell is infected, the MHC I molecules display fragments of proteins from the infectious agents to T-cells. Healthy cells do not display any proteins and will be ignored by the immune system, while the cells identified as "non-self" by foreign proteins will be attacked by the immune system.
Lymphocytes: Lymphocytes, such as NK cells, are characterized by their large nuclei that actively absorb Wright stain and, therefore, appear dark colored under a microscope.

An infected cell (or a tumor cell) is often incapable of synthesizing and displaying MHC I molecules appropriately. The metabolic resources of cells infected by some viruses produce proteins that interfere with MHC I processing and/or trafficking to the cell surface. The reduced MHC I on host cells varies from virus to virus and results from active inhibitors being produced by the viruses. This process can deplete host MHC I molecules on the cell surface, which prevents T-cells from recognizing them, but which NK cells detect as “unhealthy” or “abnormal” while searching for cellular MHC I molecules. As such, NK cells offer a complementary check for unhealthy cells, relative to T cells. Similarly, the dramatically-altered gene expression of tumor cells leads to expression of extremely-deformed or absent MHC I molecules that also signal “unhealthy” or “abnormal.”

NK cells are always active; an interaction with normal, intact MHC I molecules on a healthy cell disables the killing sequence, causing the NK cell to move on. After the NK cell detects an infected or tumor cell, its cytoplasm secretes granules comprised of perforin: a destructive protein that creates a pore in the target cell. Granzymes are released along with the perforin in the immunological synapse. A granzyme, a protease that digests cellular proteins, induces the target cell to undergo programmed cell death, or apoptosis. Phagocytic cells then digest the cell debris left behind. NK cells are constantly patrolling the body. They are an effective mechanism for controlling potential infections and preventing cancer progression.

Key Points

- Natural killer (NK) cells are lymphocytes (a subclass of white blood cells) that recognize infected or tumorogenic cells and kill them.
- Unlike the related T cells, NK cells do not recognize fragments of the infecting particle, but rather the incorrect display of major histocompatibility complex (MHC) I molecules.
- NK cells are always active, but will not perform their killing function on cells with intact MHC I molecules.
• When NK cells detect an infected or tumor cell, they secrete granules that contain perforin, creating a pore in the target cell; granzymes then pass through these pores, degrading cellular proteins, causing cells to undergo apoptosis.

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**Key Terms**

• **lymphocyte:** a type of white blood cell or leukocyte that is divided into two principal groups and a null group: B-cells, T-cells, and natural killer (NK) cells

• **major histocompatibility complex:** a protein present on the extracellular surface of the cell that displays portions of the proteins that are degraded inside the cell

• **T cell:** a lymphocyte, from the thymus, that can recognize specific antigens and can activate or deactivate other immune cells