15.4J: Cell-Mediated Immunity

The human body can respond to antigen in many different ways. These fall into two major categories:

- **antibody-mediated immunity.** Antibodies — dissolved in blood, lymph, and other body fluids — bind the antigen and trigger a response to it. (This form of immunity is also called **humoral immunity**.)
- **cell-mediated immunity (CMI).** T cells (lymphocytes) bind to the surface of other cells that display the antigen and trigger a response. The response may involve
  - other lymphocytes
  - any of the other white blood cells (leukocytes)

Examples of Cell-Mediated Immunity

**Delayed-Type Hypersensitivity (DTH): the tuberculin test**

Many states in the United States require that professors and teachers (among others) be checked periodically for tuberculosis. This chronic disease, caused by *Mycobacterium tuberculosis*, evokes an immune response that, unfortunately, does not cure the patient, but does provide an inexpensive test for the disease called the **tuberculin test** (or Mantoux test). A tiny amount of protein, extracted from the bacteria, is injected into the skin. If the subject is currently infected, or has ever been infected, with the bacteria, a positive test results. In 24 hours or so, a hard, red nodule develops at the site of the injection. This nodule is densely packed with lymphocytes and macrophages.

In Europe, most people produce a positive tuberculin reaction, not because they have had the infection, but because earlier they had been vaccinated against tuberculosis with a preparation of a related (but harmless) bacterium called **BCG**.
The response to tuberculin is called "delayed" because of the time it takes to occur (in contrast to the "immediate" responses characteristic of many antibody-mediated sensitivities like an allergic response to a bee sting).

DTH is a cell-mediated response (in fact, anti-tuberculin antibodies are rarely found in tuberculin-positive people). The T cells responsible for DTH are members of the CD4$^+$ subset.

**Contact Sensitivity**

Many people develop rashes on their skin following contact with certain chemicals. Nickel, certain dyes, and the active ingredient of the poison ivy plant are common examples. The response takes some 24 hours to occur, and like DTH, is triggered by CD4$^+$ T cells. The actual antigen is probably created by the binding of the chemical to proteins in the skin. After the antigen is engulfed by dendritic cells in the skin, they migrate to nearby lymph nodes where they present fragments of the antigen to CD4$^+$ T cells. The activated T cells migrate from the lymph nodes to the skin to elicit the inflammatory response.

**Killing intracellular parasites**

Some human pathogens avoid exposure to antibodies by taking up residence within cells. These include all viruses (discussed in the next section), and some bacteria such as

- the bacterium that causes **Legionnaires's disease**
- **Listeria monocytogenes**, that humans sometimes acquire from contaminated food and even some protozoans.

These microorganisms are engulfed by phagocytic cells, like macrophages, but evade the normal intracellular mechanisms that should destroy them. However, the macrophages can present fragments of antigens derived from these parasites. These are displayed in the class II histocompatibility molecules of the macrophages. **CD4$^+$ T cells** responding to these epitopes release lymphokines that stimulate the macrophages sufficiently that they can now begin to destroy the organisms.

**Anti-Viral Immunity**

Any cell in the body is a potential target for one kind of virus or another. However, all cells express class I histocompatibility molecules at their surface. These can display antigenic fragments of viral components. **CD8$^+$ T cells** that can bind to these epitopes can then destroy the cell (often before it can release a fresh crop of viruses to spread the infection).

**Graft Rejection**

Grafts of a kidney, heart, lung, liver, etc. from one human to another always (unless donated by an identical twin) are seen by the recipient's immune system as antigenic and elicit an immune response. If unchecked, this response will eventually lead to destruction of the graft. Both CD4$^+$ and CD8$^+$ T cells participate in graft rejection. They are responding to differences between donor and host of their class II and class I histocompatibility molecules (respectively).
Nude mice are homozygous for a gene that is essential for the development of a thymus. Lacking a thymus they cannot produce T cells and hence are unable to reject grafts. Link to a view of nude mice carrying various skin grafts without rejecting them.

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**Graft-versus-host disease**

Grafts of bone marrow are used to provide, or restore, a source of blood cells for the recipient.

For example, a number of different cancers are treated so vigorously by radiation and cytotoxic chemicals that the patient's bone marrow is destroyed in the process. Grafts of bone marrow can restore the patient. Sometimes the patient's own bone marrow — stored earlier and, if needed, treated to remove any cancer cells — is used.

Sometimes the marrow must come from another person. In this case, there is no danger of rejecting the graft because the recipient has no functioning immune system. However, if there are any histocompatibility differences between donor and recipient (and there always are some, unless the patient's own marrow is used or that of an identical twin), then the T cells of the donor will mount an immune response against the tissues of the recipient. Fortunately, graft-versus-host disease can usually be controlled with immunosuppressive drugs.

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