2.1.5

Cell-Mediated Immunity

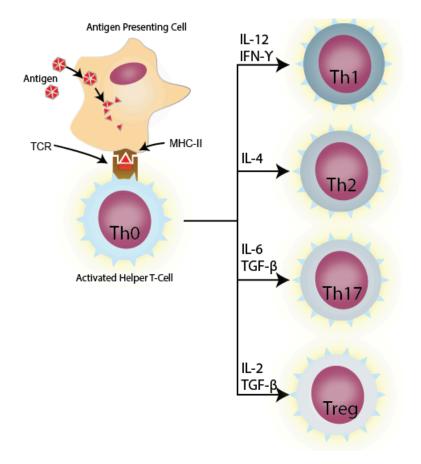
Watch the video Adaptive Immunity Part 2 - Cell-Mediated

Cell-mediated immunity is all about T-cells and begins with the activation of the helper T-cell the same way as discussed in the humoral response (which you can review in the video or the section above). To activate a cytotoxic T-cell, the same antigen fragment must also be expressed on a MHC-I receptor (recall that these are on all nucleated body cells). Once this fragment is expressed, a naïve cytotoxic T-cell with a TCR that matches the antigen present on the MHC-I will bind. CD8 expressed by the cytotoxic T-cell acts as a co-receptor and will bind to a portion of the MHC-I as well. The cytotoxic T-cell will then express cytokine receptors. The activated helper T-cell mentioned earlier will bind to receptors expressed on cytotoxic T-cells. This results in activation of the cytotoxic T-cell and causes it to proliferate to form a clone army made up of identical activated cytotoxic T-cells that will all recognize the same antigen. Some of these cells will become activated memory cytotoxic T-cells. Later in time, if the body is exposed to the same antigen, these memory cells can be quickly activated. Activated cytotoxic T-cells will recognize body cells that are infected by viruses and other intracellular pathogens by fragments expressed on their MHC-1 of the infected body cell. After binding, the cytotoxic T-cell releases perforins that will bind to the infected body cell and form pores in its plasma membrane, making it prone to lysis and death. Cytotoxic T-cells also release granzymes that induce apoptosis (programmed cell death) of the infected body cell.

Watch the video Helper T-Cells

There are several kinds of helper T-cells that allow for a more specialized immune response. The differentiation of different types of helper T-cells depends on cytokines released by the APC during the initial activation. If the APC releases IL-12, the helper T-cell will become a T-helper 1 cell or T_H1 . T_H1 specifically releases INF-gamma to macrophages and B-cells. This causes the B-cells to make IgG. T_H1 is most effective against intracellular viruses and bacteria as well as autoimmune problems. If the APC releases IL-4, the helper T-cell will become a T_H2 . T_H2 may release IL-4 to B-cells and cause a class switch to IgE. T_H2 may also release IL-5 to activate and recruit eosinophils. The final cytokine that T_H2 will release is IL-13 to stimulate mucus production in epithelial cells. T_H2 is the subtype that is found prominently in individuals suffering from allergies. These allergies are often referred to as atopic if they involve predominantly IgE antibodies. If the APC releases TGF-beta and IL-6, the helper T-cell will become T_H17 . T_H17 releases cytokines to activate monocytes (precursor to macrophages) and neutrophils.

T-regulatory cells (Treg) are also produced by the body. While research is being conducted on them, much is still unknown about these cells. For now, remember that they keep the adaptive immune cells functioning properly as well as preventing them from becoming hyperactive and causing autoimmunity. A Treg cell is made when an APC releases IL-2 and TGF-β.



Helper T-Cells and Treg Cells Image by JS F16

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	Туре І	Type II	Type III	Type IV
Immune Reactant	IgE	lgG or lgM	lgG and lgM	T cells
Timing of Reaction	Minutes to hours after antigen exposure	Variable	1 to 3 weeks after drug exposure	2 to 7 days after drug exposure
Clinical Manifestations	Anaphylaxis, hay fever, food allergies, and drug allergies	Hemolytic anemia, hemolytic disease of the newborn, neutropenia	Serum sickness, lupus, rheumatoid arthritis, vasculitis	allergic contact dermatitis, drug rash, type one diabetes, TB skin test
Mechanism of Action	lgE binds to mast cells, specific allergens then bind to IgE, inducing degranulation	IgG or IgM binds to cellular antigens, activating the complement system and causing cell lysis	Antigen-antibody complexes activate compliment and initiate the inflammitory response, recruiting neutrophils	Helper T cells react to antigens and secrete cytokines, which activate macrophages and cytotoxic T cells
Visual Representation of Mechanism	Allergen Mast cell IgE Cytokines	IgG or IqM A. NK Cell or Macrophage B. Cell lysis Cell lysis C	Antigen- antibody complex	Antigens Th Cell Cytokines Tc Cell Macrophage

The Four Types of HypersensitivityImage by Becky T F19



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