Sound the Alarm!
How the Immune System Responds

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Abstract
When antigens invade the body, molecules called macrophages envelop antigens through endocytosis and break the antigen into pieces. These fragments are handled by Class II Major Histocompatibility Complexes (MHC II), sometimes referred to as Human Leukocyte Antigens (HLA molecules). HLA-DR molecules are formed holding a placebo antigen fragment, CLIP, which maintains its structure. Inside a vesicle, an antigen fragment replaces CLIP with the help of HLA-DM, an enzyme which quickly finds the best fitting antigen fragment. HLA-DR molecules “cradle” the fragment and present it on the surface of the macrophage so that a T-cell receptor can bind to the antigen held by the HLA-DR and determine if the substance is foreign to the body. Should the substance be identified as foreign, the immune system will mount an attack against the antigen.

Step 1
A macrophage “swallows” an antigen (e.g. virus)

Step 2 Part A
Acid proteases break down the antigen into fragments

The Immune Response

Step 2 Part B
A vesicle containing HLA-DM fuses with a vesicle containing HLA-DR in its immature form with CLIP

Step 3
HLA-DM hastens the selection and placement of the best fitting antigen fragment in place of CLIP into HLA-DR, which occurs in the N terminal of the peptide

Step 4
HLA-DR moves to the plasma membrane where it will make contact with a T-cell receptor and begin the immune response

HLA-DR
- plays a vital role in the immune system of most vertebrates
- presents foreign antigens to T-cells, which either elicit or suppress T-cell responses that will lead to the production of antibodies against that particular antigen

HLA-DM
- plays a critical role in antigen presentation in the body
- helps load a peptide into HLA-DR
- catalyzes the release of the CLIP fragment from MHC class-II-CLIP complexes and discharges unstable bound peptides
- catalyzes the replacement of CLIP with a peptide from the endosome
- makes sure that the class-II molecules are capable of peptide loading and presents only highly-stable peptides (composed of alpha and beta subunits organized in a structure similar to that of the standard class-II molecules)

The Influenza Virus
~5% to 20% of Americans get the flu every year
+200,000 are hospitalized
+36,000 people die from the flu

- There are three types of influenza viruses: A, B and C, all of which can alter its genetic composition over time
- Influenza type A divided into subtypes based on two proteins on the virus’ surface: hemagglutinin (H) and neuraminidase (N); e.g. (H1N1) and (H3N2) found in many different animals (ducks, chickens, pigs, whales, horses, and seals)
- Influenza type B not divided into subtypes circulate widely only among humans

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