WHAT THE IMMUNE SYSTEM IS RECOGNIZING TOWARDS THE NEW PARADIGM

Summary

Individuals are protected against infections by two mechanisms. The first one non-specific, innate immunity which provides an early protection and is executed mainly by phagocytic cells, and the later one developing specific adoptive immunity which depends on B and T lymphocytes equipped in clonally distributed antigen-specific receptors. T cells recognize an antigen only when presented by the antigen presenting cells (APC), i.e. B lymphocytes, macrophages or dendritic cells (APC) (Signal I). APCs in turn produce an array of different mediators that stimulate T cells to perform their antigen-specific functions (Signal II). As shown by C. A. Janeway, APCs produce Signal II only upon recognition of highly conserved structures (patterns) on the surface of pathogens (PAMPs) by cell-membrane bound non-clonal wide-specific receptors (PRR) (e.g. toll-like receptors, TLR). Only then they decide whether the specific immune response will be induced at all, and also determine the type of effector mechanisms (humoral or cellular). In the "danger hypothesis" by P. Matzinger, more important than recognition of a foreign antigen is recognition of danger signals produced by cells exposed to different kinds of stress (e.g. heat shock proteins, HSP). These signals then activate APCs that, in turn, present antigen to lymphocytes. Antigens that do not cause cell damage (including also some bacterial antigens) are non-immunogenic. Moreover, the effector mechanisms triggered by an antigen are determined not by the antigen itself but by signals flowing from tissues in which antigen is recognized. These models are not mutually exclusive. The integrative hypothesis stresses the role of both microbial products and endogenous macromolecules in activation of the immune surveillance.