

Cross presentation and Immune surveillance.

Kenneth L. Rock, M.D.
UMass Medical School
Worcester, MA 01655

In all tissues there are sentinel cells of bone marrow origin whose role is to collect antigens in the tissues and report their presence to T lymphocytes. These sentinels, the most important of which are dendritic cells, play an essential role in the generation of CD8 T cell immune responses. In their absence, the immune system is not able to respond to or even detect most cancers or viral infections. Dendritic cells have evolved specialized mechanisms that allow them to acquire tissue antigens and present them to T cells. However, while this process of acquiring and displaying antigen is necessary for immune surveillance, it is not sufficient. The sentinel cells must also become activated, which occurs when they sense that the antigens they are collecting are associated with a situation that is dangerous for the host. Some danger signals are components of pathogens while others are generated by host cells. Once CD8 T cells are stimulated by antigen presenting cells to become effector lymphocytes they circulate in search of the cells that are producing the immunogenic antigen. These antigen-producing cells are identified through their display on the cell surface of antigenic peptides bound to MHC class I molecules. The MHC class I-presented peptides are generated through a process that can involve multiple distinct proteolytic steps, each of which may have distinct specificity. As a consequence of these mechanisms only a fraction of the potential epitopes within an antigen. The mechanisms underlying several of these processes will be discussed.