

Immune surveillance of tumors and immunodominance of responses

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Abstract

To generate a CD8 T-cell response to a tumor, antigens must be acquired and presented on MHC class I molecules of bone marrow-derived antigen presenting cells (APC) such as dendritic cells. This occurs through a process termed cross presentation that can involve a number of distinct intracellular pathways. The APC must also be stimulated in ways that cause them to become competent to activate naïve T cells and migrate to secondary lymphoid tissues. This stimulation can be provided by endogenous or exogenous adjuvants together with signals provided by lymphocytes.

Once CD8 T cells are stimulated by APC to become effector T cells they circulate in search of the offending cells that are producing tumor antigen. Such tumor 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 up to five distinct steps, each of which may have distinct specificity. As a consequence of these mechanism only a fraction of the potential epitopes within a tumor antigen are actually presented and this constrained repertoire of presented peptides contributes substantially to narrowing the specificity of the T cell immune response (aka the phenomenon of immunodominance). Constraints of antigen presentation affect not only the specificity of the primary T-cell response but also that of recall responses.