Unique functions of splenic CD8alpha+ dendritic cells during infection with intracellular pathogens.

Abstract: Deciphering the prerequisites for the induction of protective cytotoxic T cell responses is essential for future development of more effective CD8(+) T cell-based vaccines against infectious diseases and cancer. Since crucial events for CD8(+) T cell priming and differentiation occur during the first contacts of naïve T cells with distinct antigen-presenting cells (APCs), the identification and therapeutic targeting of these 'master' APCs has become a major quest in the field. A decade ago, dendritic cells (DCs) were discovered as potent APCs, as they combine all major features for the initiation of T cell responses: (1) naïve DCs demonstrate high endocytic activity and scan continuously their environment in strategic positions throughout the whole body; (2) after activation (e.g. during pathogen invasion), DCs migrate into T cell zones of their draining lymphatic compartments, meanwhile processing captured antigen and maturing in order to stimulate encountered antigen-specific T cells. During the last years, different subsets of DCs that can be distinguished by specific surface marker expression and effector functions have been identified in mice. Their distinct functional capabilities have led to the concept of work-sharing; "migrating" DCs primarily transport antigens to the lymph node, where a specialized subset of "resident" DCs, defined by the expression of the CD8alphaalpha homodimer (CD8alpha(+) DCs), primes CD8(+) T cells upon antigen
cross-presentation. Accordingly, CD8alpha(+) DCs have been found to prime CD8(+T cells against different viruses as well as intracellular bacteria such as Listeria monocytogenes (L.m.). Recently, L.m. was found to survive specifically in splenic CD8alpha(+) DCs shortly after intravenous infection. Further experiments revealed a more generalized sampling activity of CD8alpha(+) DCs for blood-borne particles. These findings indicate that splenic CD8alpha(+) DCs might unite efficacious antigen-trapping with the licence to prime CD8(+T cells. This new aspect of DC function could have evolved to guarantee a more rapid antigen-specific response against generalized infections.