ELSEVIER

Seminars in Immunology 17 (2005) 251–252

seminars in
IMMUNOLOGY

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Introduction

Dendritic cell heterogeneity: Developmental plasticity and functional diversity

Dendritic cells (DCs) are essential elements of the immune system due to their capacity to participate not only in primitive defense mechanisms that constitute the innate immunity, but also in the induction and regulation of antigen-specific immune responses. This multiple functional potential allows DCs to control parasitic and microbial infections as well as tumor growth; to exert a precise regulation of T cell, B cell and NK cell immune responses; and to induce and maintain T cell tolerance, needed to neutralize autoreactive T cells.

Research performed over the last decade has evidenced that the functional diversity displayed by the DC system relies essentially on the remarkable plasticity that characterizes the DC differentiation process. This determines the acquisition of DC functional specialization through the generation of a large collection of DC subpopulations, located in both non-lymphoid tissues and lymphoid organs. Studies mainly performed in the murine system have shown that certain DC subpopulations (e.g. $CD8^-$ DCs, $CD8^+$ DCs or $B220^+$ plasmacytoid DCs) can be found in different locations (e.g. thymus, spleen, lymph nodes or Peyer's patches), whereas other DC subpopulations appear to be organ-specific (e.g. skin Langerhans cells or $CD8^-$ $CD11b^-$ DCs intestinal DCs).

DC development has been demonstrated to proceed from both myeloid and lymphoid progenitors through multiple differentiation pathways, through yet non-fully defined immediate DC precursor populations. On the other hand, the differentiation of DCs, in contrast to that of other hematopoietic cell lineages (that differentiate almost exclusively in the bone marrow and thymus), mostly occurs by recruitment of these immediate DC precursors to the effector sites where DCs exert their specific function. These immediate DC precursors then differentiate locally into defined DC subpopulations endowed with specific functional abilities, under the influence of precise chemotactic and differentiation factors. Acquisition of DC functional diversity is not only achieved during the differentiation process under the control of local factors, but can be further determined by the activation stimuli to which differentiated DCs can be subjected during the induction of the DC maturation phase. Therefore, the functional diversity displayed by the different DC subpopulations present in non-lymphoid tissues and in lymphoid organs relies in the developmental and homing potential of their immediate precursors; the local differentiation factors these immediate precursors will encounter upon recruitment to a defined effector site; and the activation stimuli promoting the maturation of each DC subpopulation.

This volume assembles seven manuscripts that summarize current knowledge on the different DC subpopulations that integrate the DC system, including the DC subsets located in the thymus, skin, lymph nodes, spleen, intestine and lung mucosal lymphoid tissues, plasmacytoid DCs and monocyte-derived DCs. In particular, the differential potential and functional relevance of these DC subpopulations regarding a number of essential immunological functions of DCs, have been considered. These include the migration to non-inflammatory or inflammatory locations; the capture and processing of different parasitic and microbial pathogens; the induction of immunogenic or tolerogenic responses; the polarization of T helper responses towards a Th1 or Th2 profile; the activation of CTL and B cell differentiation; and the stimulation of NK cell function.

However, although these reviews reveal the enormous progress achieved on the study of DC biology over the last few years, a number of unknown essential issues have to be addressed regarding the function of the different DC subpopulations that constitute the DC system. These include the characterization of the immediate precursors for each DC subpopulation and how their differentiation is controlled; the definition of the receptors for chemotaxis, antigen capture and activation expressed by DC subpopulations and how the signalling pathways mediated by these receptors are integrated; the analysis of the maturation and migration behaviour of the different DC subpopulations during the induction of an immune response; and the characterization of the mechanisms responsible for the functional cooperation between DC subpopulations.

1044-5323/$ – see front matter
doi:10.1016/j.smim.2005.05.014

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