DENDRITIC CELLS IN THE INDUCTION OF IMMUNITY

Stella C. Knight
Division of Immunological Medicine
MRC Clinical Research Centre
Watford Road, Harrow, Middlesex HA1 3UJ, UK

INTRODUCTION

Bone marrow-derived dendritic cells (DC) are potent antigen-presenting cells and are particularly important for their capacity to recruit resting T cells into immune responses (Metlay et al, 1990; Melief 1989). An outline of the life history of DC is shown in Fig. 1. The macrophage and dendritic cell lineages diverge early from a bone-marrow stem cell (Reid et al, 1990) and occasional stem cells (Reid et al, 1990) as well as more mature DC (Steinman, 1989) are also present in peripheral blood. There is evidence that DC may enter the spleen directly and they are also distributed in small numbers to most tissues of the body. The tissue specific stage of their life history is exemplified by the skin Langerhans' cells. In the tissues, the DC appear to act as sentinels of the immune system and, particularly following exposure to antigen, can travel as veiled cells in the afferent lymphatics to the lymph nodes where many may localise in the T dependent, paracortical areas. There is strong circumstantial evidence that they

![Fig. 1. Dendritic cell life history.](image-url)
Bone marrow-derived dendritic cells in peripheral tissues exemplified by Langerhans' cells (LC) of the skin can acquire antigen, travel as veiled cells (VC) in the afferent lymphatics and become interdigitating cells (IDC) of the paracortex of lymph nodes. These cells may stimulate T4 and T8 cells directly. Antigen-antibody complexes formed during secondary exposure can be trapped by follicular dendritic cells (FDC) and are important in stimulating B cell memory.

It is not clear whether DC from tissues can re-enter the circulation but there is little evidence of DC leaving the lymph nodes in afferent lymph. It is believed that they end their life in the nodes, perhaps through killing by natural killer cells (Shah et al., 1985) or by a specific T cell dependent cytotoxic effect (Macatonia, Taylor, Askonas and Knight, in preparation).

DC isolated from lymph nodes or spleen are able to cluster T cells non-specifically. This distinguishes them from antigen-bearing macrophages which are only able to cluster T cells specifically responding to the antigen. The capacity of DC to cluster T cells non-specifically and then to retain and activate specific cells is consistent with their peculiar ability to recruit resting T cells into immune responses. Both T4 and T8 cells can be activated by DC (Macatonia et al., 1989) (Fig. 2). Once T cells are activated there are many other cells bearing MHC class II molecules that are able to promote the growth of these pre-activated clones. Within the lymph nodes the role of follicular dendritic cells (a different cell lineage, probably derived in situ from fibroblastic elements within the lymph nodes) in memory responses is established (Tew et al., 1989). These follicular cells are believed to acquire antigen/antibody complexes and activate B cells which in turn can promote the T cells responses (Fig. 2). There are suggestions that activated B cells may be able to initiate resting T cell responses to some extent (Metlay et al., 1990). However, in our studies of contact sensitizers and influenza virus in mice we found no evidence that B cells from the lymph nodes stimulated T cell responses (Tew et al., 1989) and the major route of stimulation was via the bone-marrow-derived DC.