atopoiesis (19–28); and (9) the observation that a number of physical (e.g., ultraviolet radiation, heat, surgical trauma) and chemical (e.g., steroids, arachidonic acid, transdermal delivery systems) agents can have profound effects on the generation of immune responses to antigens first encountered through the skin (29–32). Thus, by affecting any of the various components of SALT the normal immunological capacity of the skin can be changed, with the potential for altering not only local, but also systemic, immune responses.

The peripheral secondary lymphoid tissues that drain the skin provide the necessary immunological environment for the induction of an immune response. Antigens first encountered through the skin are transported to the draining lymph nodes by epidermal Langerhans cells and macrophages through the afferent lymphatics (33). In contrast, more than 90% of the lymphoid cells that enter the lymph nodes do so from the blood stream. The entry of T cells from the circulation into peripheral lymph nodes is mediated and regulated by specific interactions between the T cells and anatomically distinct sites of the cuboidal endothelial cell-lined postcapillary venules, the so-called high endothelial venules (HEV; 34). After binding to HEV, lymphocytes are able to extravasate from the circulation and enter the parenchyma of the lymph node (35).

Events that affect skin can have profound effects on the SALT circuit. For example, Spangrude et al. found that the number of radiolabeled murine T cells that "homed" to peripheral lymph nodes rose from 11.1% in control mice to 21.8% in mice exposed to 5000 J/m^2 per day of UVB radiation over a period of 6 days (36). Furthermore, this alteration in the lymphocyte trafficking pattern was observed to persist for up to 2 months. The increase in the numbers of T cells homing to peripheral lymph nodes in UV-irradiated mice appears to be due to many factors. For example, increases in HEV structure and function have been observed in the peripheral lymph nodes of mice exposed to relatively modest doses of UVB radiation (37). This may well be due to an increase in the number of activated APC in the peripheral lymph nodes as well as an increase in the production of cytokines, such as interleukin-1 (IL-1), by UV-irradiated keratinocytes (38). The situation is further accentuated by the effects of increased production of prostaglandins during the inflammatory response induced by UV exposure. The increased release of prostaglandin produces an efferent lymphatic blockade that, in turn, leads to increased retention times for recirculating lymphocytes in the lymph nodes (39). It is important to note that the changes in lymphocyte recirculation patterns produced by short-term exposure to UV radiation are similar to those caused by cutaneous administration of antigen (40). Whether similar changes are