events.

Most recently, Scholzen *et al.*[33] demonstrated that CH was enhanced in neuropeptidase-knock out mice. It is noteworthy that this effect could be abrogated by injections of a neurokinin-1 receptor (NK-1R)-specific antagonist.[33] This result enables us to postulate that enhancement of signals through NK-1R could enhance CH response by blocking degradation of SP.

Concluding Remarks

The deleterious effects of UVR on cutaneous immunity include failed CH induction, promotion of hapten-specific tolerance, and creation of a systemic immune deficiency. Recent studies on the mechanism of action of UVR have revealed that two cell types not originally included in the SALT concept are important: mast cells and cutaneous nerves. It now appears that mast cells serve as a reservoir of immunomodulatory cytokines. Under normal conditions, *i.e.* when SALT functions normally, immunization through the skin avoids release of these cytokines from mast cells and local and systemic CH emerges. At the same time, neuropeptides stored in cutaneous nerves contain both positive and negative regulators of cutaneous immunity. CGRP appears to function as the chemical messenger, released from UVR-exposed nerve endings, that triggers mast cells to release TNF-α, and thereby engenders the altered immunity. SP, by contrast, has the capacity to promote the induction of CH. The precise cellular target of SP in promoting CH induction is not known, but the fact that nerve termini abut directly on the surface of LC suggests that these APC may act on a SP signal. We have no idea how and why SP acts in normal skin to promote and enhance CH induction, especially since both SP and CGRP are simultaneously released from cutaneous nerves. Perhaps haptens cause the selective release of SP, and unsuppressed CH results, whereas UVR causes the release of both CGRP and SP, and only the former survives long enough to trigger mast cell degranulation. Since Paul Langerhans began the inquiry into the cells that bear his name more than a century ago, there is a kind of poetic justice in the recent realization that cutaneous nerves acting directly or indirectly on LC dictate whether antigen applied to or arising within skin will lead to sensitivity or tolerance.

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