DENDRITIC CELLS

New DCs found deep in the skin

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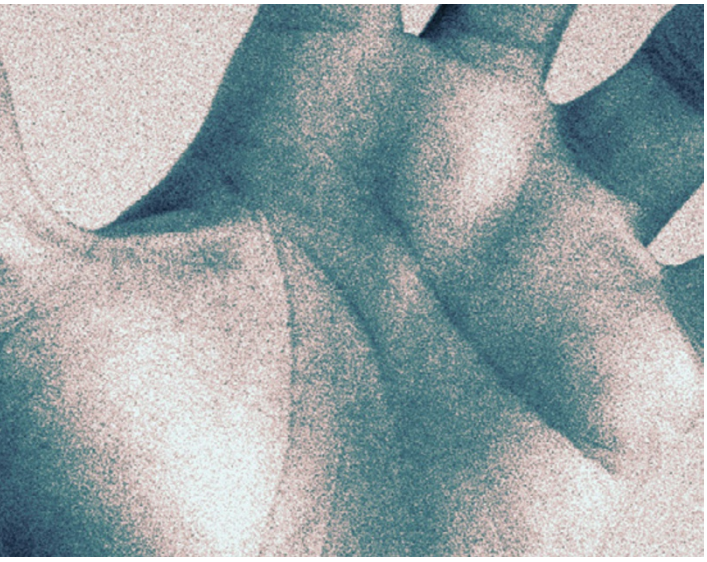
Langerhans cells (LCs) are a subset of dendritic cells (DCs) that express the C-type lectin langerin (also known as CD207) and reside as immature cells in the epidermis of the skin. Following interaction with pathogens, LCs mature and migrate via lymphatics to the T-cell-rich areas of draining lymph nodes (DLNs). Now, three studies have identified a new population of langerin$^+$ DCs that reside in the dermis of the skin and that arise from a different developmental pathway compared with LCs.

Previous studies have shown that epidermal LCs are radioresistant cells and therefore remain host-cell-derived following irradiation in the generation of bone-marrow chimaeras. By contrast, all other DC populations are radiosensitive and are donor-cell-derived in bone-marrow chimaeras.

Poulin *et al.* generated chimeric mice by irradiating recipient mice and reconstituting them with bone-marrow cells from mice in which the expression of enhanced green fluorescent protein (EGFP) was under the control of the langerin promoter. Unexpectedly, when they analysed cells from cutaneous DLNs in the chimeric mice, in addition to the anticipated population of EGFP$^-$ (that is, of host origin) radioresistant cells derived from migratory epidermal LCs, they also identified a population of EGFP$^+$ donor-cell-derived DCs (that is, the host cells were radiosensitive). This new type of DC, which is langerin$^+$, resides in the dermis, has a rapid turnover and, following ablation, repopulates the dermis and the DLNs at a much faster rate than the LCs. So, whereas LCs are langerin$^+$ radioresistant cells that reside in the epidermis, this new type of DC subset, which the authors refer to as langerin$^+$ dermal DCs, is radiosensitive.



Ginhoux and colleagues used the same mouse model system, but in this case taking advantage of the fact that in addition to EGFP the mice also express the diphtheria toxin receptor under the control of the langerin promoter. In these mice diphtheria toxin administration efficiently eliminated all langerin$^+$ cells. After diphtheria toxin administration, langerin$^+$ DCs were shown to repopulate the cutaneous DLNs (these cells were previously thought to be trafficked LC-derived cells) and the dermis long before the reappearance of LCs in the epidermis, suggesting the existence of a population of non-LC-derived langerin$^+$ DCs. Further work showed that these langerin$^+$ DCs are derived from bone-marrow precursors that can seed both the dermis and the DLNs. The authors also showed that langerin$^+$ DC precursors depend on endothelial-cell selectins and CC-chemokine receptor 2 (CCR2) to seed the dermis and on CCR7 to migrate to the cutaneous DLNs. Both langerin$^+$ DCs and LCs were shown to patrol the skin and convey antigenic information to cells in the DLNs.

Similar to the other studies, Bursch *et al.* identified a new population of langerin$^+$ DCs in the dermis of the skin, which was also present in other tissues, particularly in the lungs. In addition, they tested the function of these cells in skin immune responses by performing contact hypersensitivity (CHS) assays in mice in which langerin$^+$ cells had been ablated using treatment with diphtheria toxin. In these mice, dermal langerin$^+$ DCs reappear in the dermis within 3 days of treatment with diphtheria toxin, whereas LCs were not detectable in the epidermis until a much later time point. This difference in repopulation kinetics allowed the authors to specifically assess the role of dermal langerin$^+$ DCs in CHS responses. They found that dermal langerin$^+$ DCs are necessary for optimal CHS responses and can promote these responses in the absence of epidermal LCs.

Taken together, these three studies identify a new population of dermal langerin$^+$ DCs and they help clarify some of the confusing results derived from previous studies when the existence of these cells was unappreciated.

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ORIGINAL RESEARCH PAPERS Poulin, L. F. *et al.* The dermis contains langerin$^+$ dendritic cells that develop and function independently of epidermal Langerhans cells. *J. Exp. Med.* **204**, 3119–3131 (2007) | Ginhoux, F. *et al.* Blood-derived dermal langerin$^+$ dendritic cells survey the skin in the steady state. *J. Exp. Med.* **204**, 3133–3146 (2007) | Bursch, L. S. *et al.* Identification of a novel population of Langerin$^+$ dendritic cells. *J. Exp. Med.* **204**, 3147–3156 (2007)