Einwanderung von Langerhanszellvorläufern in die Epidermis: Entwicklung eines Modellsystems

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2000

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urn:nbn:at:at-ubi:2-12690

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Langerhans cells are a well examined part of the dendritic cell system of professional antigen presenting cells. Together with all other dendritic cells they have the unique capacity to stimulate naive T cells and thereby are at the beginning of almost all acquired immune responses. In this work the migration behaviour of dendritic and Langerhans cells was studied in the murine system, particularly with regard to the immigration of Langerhans cell progenitors into the epidermis.

In a first approach immature and mature bone marrow-derived dendritic cells, labelled with PKH26 were injected intravenously into BALB/c mice. In preliminary experiments PKH26, an fluorescent cell linker, was extensively tested as for being suitable for dendritic cell migration experiments. At defined time points after injection lymphoid organs (spleen, mesenterial lymph nodes, bone marrow), epidermis and dermis were prepared and analysed for the presence of fluorescent cells.

Bone marrow-derived dendritic cells preferentially homed to spleen, the first lymphoid organ encountered, followed by a discrete number in the bone marrow, most probably pluripotent stem cells, and only single dendritic cells in the mesenterial lymph nodes. As long as the lymphoid organs were examined it could be observed, that dendritic cells homed to their destination site and stayed there. Experimental evidence suggested that the stem cells that homed to the bone marrow subsequently divided and gave raise to a novel $PKH26^+$ dendritic cell population that could be detected in all lymphoid organs examined around day 18 after injection. Interestingly, there were no differences between the maturation stages.

No intravenously injected $PKH26^+$ cells were found in the skin, probably because cells able to home to the epidermis were retained by the lung epithelium, that also contains dendritic cells similar to Langerhans cells.

Concentrating on the epidermis, in a second approach we established a model in which a demand for Langerhans cells was created in the epidermis by a novel gentle tape stripping-technique. This technique depleted the epidermis of Langerhans cells by mimicking the inflammation that often occurs with antigen-uptake, that led to the emigration of Langerhans cells from the epidermis. The epidermis was not severely damaged, as in previously described experimental settings (171,178,205). Intradermal injection of immature bone marrow-derived dendritic cells was chosen as administration route to circumvent the lung epithelium. Two days after injection into tape-stripped ears up to 300 times more Langerhans cells, selectively stained for their MHC class II molecule-haplotype, were detected in the epidermis, as compared to untreated ears. These results confirmed that a demand for Langerhans cells is needed to allow new immigration of precursor cells. Already on day 3 after injection the number of injected cells decreased to lower levels, still detectable on day 10.

We have established a suitable *in vivo* model for studying the immigration of Langerhans cells into the epidermis, with which chemokines and cytokines apparently involved in migration and skin homing of Langerhans cells can be tested in future experiments. Their ability to modulate Langerhans cell numbers detected in the skin and their influence on the time course would be of interest.