

The Migration Route of Langerhans Cell

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Introduction

Langerhans cells are one kind of Dendritic Cells (DCs) playing some roles in immune systems, the most essential role is presenting antigen's information to T cells. When foreign substances go into the skin, LCs capture these and migrate with their information to the draining lymph vessels. Finally, LCs present the antigen's peptide to T cells in the lymph nodes.

The route of LCs migration could be two ways, not only via lymph vessels but also vein vessels. In this time, I present about migration of LCs.

1. LCs migrate from the skin via lymph vessels.
2. LCs migrate to the immune tissue via vein vessels.

1. LCs migrate from the skin via lymph vessels – Investigating by using human and mice tissue-

(1) The fact, that LCs migrate via lymph vessels, is true

In the hematoxylin-eosin-stained specimens of human seborrheic keratosis tissue, I found a few LCs in the lymph vessels of this dermis. These LCs were CD1a- and S-100-

positive, showing a dendritic pattern by immunohistopathological studying. These results indicate that immature CD1a-positive LCs in the skin capture antigens and migrate for delivering the antigens' peptides from the skin via afferent lymph vessels. These LCs in the lymph vessels could be mature. It is thus apparent that LCs bearing antigen's information migrate via lymph vessels from the skin.

(2) Where did LCs go to?

I conducted patch testing using mites antigen labeled with PKH26 dye in atopic model, NC mice (Nisiki mice with cinnamon color) for investigating this question. I excised some skin specimens from the patch-testing sites and some regional lymph nodes (inguinal and axil) at 0.5, 1, 3, 6, 9, 24, 48, 72 and 168 hours after the patch testing. The results showed that the number of LCs in the patch testing sites at 48-hour and at 72-hour by immunohistochemical study using protein kinase C-II (PKC-II) staining as a marker of LCs were significantly decreased by 13.7% ($p < 0.05$) at 48-hour sites and by 17.6% ($p < 0.05$) at 72-hour sites respectively compared to negative control. At 24-, 48-, 72- and 168-hour after patch testing, there were some LCs expressed PKH26 dye in the T-cell area, sinus and marginal area in the regional lymph nodes. In the B-cell areas of these lymph nodes, there were not any PKH26 dye-positive spots, it looked dark and round-shaped. I found that PKC-II positive LCs labeled with PKH26 dye in the lymph nodes possessed a few rod-shaped atypical granules by electron microscopy. Birbeck granules (BGs) and atypical granules (racket-shaped and rod-shaped cytoplasmic granules) are features of LCs. Atypical granules had triple-layered limiting

membrane in the Golgi area, these function were unknown. This study demonstrated that LCs captured and processed antigens, and LCs bearing antigens migrated to the lymph nodes for presenting the antigens' information to T cells.

(3) How to induce migration of LCs?

Granulocyte-macrophage colony-stimulating factor (GM-CSF) is an important factor in the viability and function of LCs. When irritant substances adhere to the skin, the irritant substances stimulate keratinocytes. Active keratinocytes produce GM-CSF, which induces the maturation and migration of LCs. Our research showed that the level of GM-CSF in the skin of patch-testing sites increased with time, and the peak of the GM-CSF levels was at a 48-hour site after patch testing, then the GM-CSF levels decreased. The migration of LCs was initiated by GM-CSF after activating keratinocytes.

2. LCs migrate to the immune tissue via vein vessels.

By examining seborrheic keratosis using immunohistochemical study with CD1a and CD83 antigen, I observed that some

CD1a- and CD83-positive LCs passing through the valve of the vein in the dermal layer of this skin. These findings suggest that some mature LCs in the epidermis migrate via vein vessels. In another my investigation, I found CD83-positive LCs in normal human lung, since some LCs in the veins could migrate to the lungs. LCs after migration play essential roles in the immune system of the lung. Both skin and lungs have contact with the outside world of the body, and these tissues could share common irritant substance's information. Another possible reason for the LCs migration via veins is presenting antigen's information to T cells in the peripheral blood vessels. I suspect that some LCs in the veins might migrate to the various tissues and present antigen's information to T cells.

Conclusion

Thus, the route of LCs migration is not only via lymph vessels but also the veins, and CD83- and CD1a-positive mature LCs may be present in the peripheral blood. These LCs moving were initiated by GM-CSF.