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## Langerhans Cells Could Migrate via Vein

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### ABSTRACT

The aim of this study is to investigate other route for LCs migration. Generally, Langerhans Cells (LCs) capture some antigens, then LCs migrate from the skin and present antigen to T cells in the lymph nodes. The priority route of LCs migration is via lymph vessels. If some of LCs migrates via veins, some of these cells could go to other organs, for instance, lung. We have investigated human cutaneous tissue, seborrheic keratosis by hematoxylin-eosin and immunohistochemical studying for the relation between LCs and seborrheic keratosis. We used 3-step ABC technique for CD83 and S-100 staining and LSAB technique for CD1a. We observed many s-100 and CD1a positive LCs were in the epidermis, some of these were CD83 positive cells in the vein of the dermis. One of them was passing through the valve of the vein. This was a CD83 positive cell. Present findings supported that some LCs could migrate via vein vessels. Both skin and lung have been in contact with the outside world and could have common information about antigen. Some LCs in the vein might migrate to the lung and present some information about antigens to T cells in the lung. We concluded that the route of LCs migration is not only via lymph vessels but also via the veins.

**Key words:** Antigen-Presenting-Cells (APC), Langerhans Cell (LCs), migration, vein, CD1a and CD83

### INTRODUCTION

Dendritic cells are antigen-presenting cells in the skin and other organ tissues. Langerhans Cells (LCs) are a kind of dendritic cells derived from bone marrow in the skin. LCs plays some essential roles and LCs has close relations to allergic skin reactions, especially in the delayed hypersensitivity skin reaction. A previous report showed (Kripke *et al.*, 1990) that Ia positive cells and FITC positive cells, some of which are LCs, leave the skin after epicutaneous sensitization and participate in the initiation of the contact hypersensitivity response in the regional lymph node. LCs migrate via lymph vessels from the skin (Sugiura *et al.*, 2003) and then LCs present antigen-peptide to helper T cells in the lymph nodes (Sallusto and Lanzavecchia, 1999; Banchereau and Steinman, 1998). Generally, LCs in the skin is immature cells (Inaba *et al.*, 1986) and then migrates from the skin with maturation to the lymph nodes (Yanagihara *et al.*, 1998; Weinlich *et al.*, 1998). Kobayashi and Hashimoto (1983) reported that LCs containing BGs migrated from dermis into the paracortical area of draining lymph nodes after injection of sterile saline in to the skin. The features of mature LCs are Birbeck Granules (Bgs). BGs are racket-shaped and rod-shaped cytoplasmic granules in the Golgi area, their functions are unknown.

Kelly *et al.* (1978) reported that a number of large mononuclear cells with ruffled surface membranes travel from the skin, via the lymphatics, to the draining lymph node. About 3% of these cells contain BGs and isotopes labeling the majority of lymph-borne mononuclear cells were detected in the lymph node within at most 24 h in the rabbit (Kelly *et al.*, 1978). Atypical granules show in immature LCs and atypical granules are going to turn into BGs with maturation of LCs (Mikihiro, 1970). We have ever studied about LCs in the skin tumors; in this time we observed CD1a and CD83 positive cells in the vein of the dermis. Because CD1a and CD11c positive cells were in the peripheral blood (Ito *et al.*, 1999), it is a strong possibility that some LCs migrate from the skin via vein vessels from our results.

## **MATERIALS AND METHODS**

This study was conducted from April 2009 to July 2010 at our clinic.

**Skin:** We gave informed consent to all patients in writing and obtained seborrheic keratosis by the skin surgery. We fixed them in 10% formaldehyde. We routinely processed and embedded with paraffin.

**Antibody:** CD1a (Immunotech, Marseilles, France), CD 83 (Biotech, Oxfordshire, UK), S-100 (DAKO Diagnostics, Humburg, Germany).

**Staining:** We cut skin specimens at 3  $\mu$ m serially and routinely stained one serial section of these skin specimens with Hematoxylin-Eosin (HE).

**Immunohistochemical studying:** We prepared three serious sections for immunostaining. We used 3-step avidin-biotin complex (ABC) (Vector CA, USA) technique for CD83 staining and S-100 staining and labelled streptavidin biotin (LSAB) (Bio Genex CA, USA) technique for CD1a. Staining for CD1a was done by 3-amino-9-ethylcarbazole (AEC) and for S-100 and CD83 by 3, 3'-diaminobenzidine tetra-hydrochloride (DAB).

## **RESULTS AND DISCUSSION**

We observed some s-100 and CD1a positive cells with dendritic pattern in the vein of the dermis. One of them was passing through the valve of the vein. This was a CD83 positive cell (Fig. 1).

Langerhans Cells (LCs) play important roles in immune cutaneous, thymus, lung and lymph nodes systems. The epidermis of 4-5% is composed by LCs. We observed CD1a LCs in the vein by immunohistochemical studying. It is necessary to confirm why a CD1a and CD83 positive LC was in the vein. We guessed three reasons: the first is that they are presenting antigen to the T lymphocytes in the vein, second is that they are presenting information about antigens to the lung immune systems and third is wrong migration. There were some reports about Airborne Contact Dermatitis (ACD) (Bonamonte *et al.*, 2002; Patiwael *et al.*, 2005). Respiratory symptoms after skin prick test and pollen allergy causing skin irritation were common findings. These symptoms were often caused at a different site to the one where the antigens were introduced. It is our hypothesis that some LCs in the veins could be one causative factor in the ACD and these symptoms. Previously some investigators studied CD1a positive LCs in the lung by immunohistochemical method (Fox *et al.*, 1989; Coli *et al.*, 1990). It is a possibility that some LCs migrate from the skin

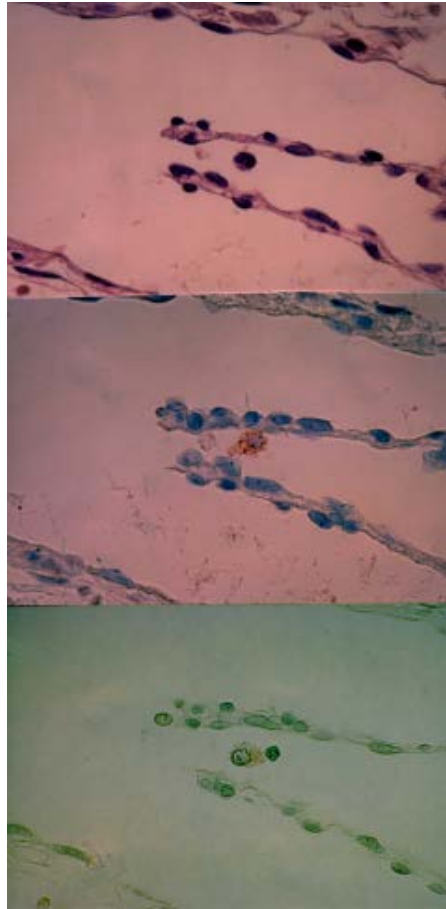


Fig. 1: Upper side, HE staining of the skin, original magnification  $\times 100$  Middle side, CD1a staining of the skin, original magnification  $\times 100$  Lower side, CD83 staining of the skin, original magnification  $\times 100$

to other organs, especially lung and present common information about the antigens to the immune systems. We assured the above mentioned first and second reasons for CD1a and CD83 (+) cells in the vein to be true. Migration of LCs was induced by some chemokines (Zaitseva *et al.*, 1997; Sato *et al.*, 1999; Dieu *et al.*, 1998) and cytokines (Heufler *et al.*, 1988; Cumberbatch *et al.*, 1997; Roake *et al.*, 1995). It is unknown that what kinds of chemokine caused migration via vein, but same cytokines and chemokines would play roles in migration via vein. Complements are important signals for allergic hypersensitivity, interaction between mast cells and dendritic cells (Jawdat *et al.*, 2004). Mast cells induce LCs migration through mast cell derived signals and histamine (Caron *et al.*, 2001a, b; Jawdat *et al.*, 2004) and IgE mediated mast cell activation induced Lcs migration (Jawdat *et al.*, 2004). Because there were many mast cells, H2 receptors and a lot of histamine in the vein, these could be related with LCs migration via vein. Our conclusion was that the process and route for LCs migration from the skin may not only be via lymph vessels, but also via veins.

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