

## Regulation of the Regeneration of Epidermal Langerhans Cells by Stress Hormone

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**Abstract :** Epidermal Langerhans cells reside in upper layer of epidermis and play a role in immune surveillance. The finding of the close association of nerve endings to Langerhans cells triggered the research on systemic regulation of Langerhans cells. They disappear from epidermis after exposure to environmental and internal stimuli and reappear about a week later. Myeloid progenitor cells are assumed to be one of the sources of Langerhans cells. We examined the effects of cortisol on the reappearance of Langerhans cells in vitro. Cord-blood derived CD34-positive cells were cultured in the medium supplemented with stem cell factor/Flt3 ligand/granulocyte macrophage-colony stimulating factor/tumor necrosis factor alpha/bone morphologic protein 7/transforming growth factor beta in the presence or absence of cortisol. Cells were analyzed by flow cytometry for CD1a (cluster differentiation 1a), a marker of Langerhans cells and dermal dendritic cells, and CD39 (cluster differentiation factor 39), extracellular adenosine triphosphatase. Both CD1a-positive cells and CD39-positive cells were decreased by treatment with cortisol (suppression by 35% and 22% compared to no stress hormone, respectively). Differentiated Langerhans cells are attracted to epidermis by chemokines that are secreted from keratinocytes. Epidermal keratinocytes were cultured in the presence or absence of cortisol and analyzed for the expression of CCL2 (C-C motif chemokine ligand 2) and CCL20 (C-C motif chemokine ligand 20), which are typical attractants of Langerhans cells, by quantitative reverse transcriptase polymerase chain reaction. The expression of both chemokines, CCL2 and CCL20, were suppressed by treatment with cortisol (suppression by 38% and 48% compared to no stress hormone, respectively). We examined the possible regulation of the suppression by cortisol with plant extracts. The extracts of Ganoderma lucidum and Iris protected the suppression of the differentiation to CD39-positive cells and also the suppression of the gene expression of LC-chemoattractants. These results suggest that cortisol, which is either systemic or locally produced, blocks the supply of epidermal Langerhans cells at 2 steps, differentiation from the precursor and attraction to epidermis. The suppression is possibly blocked by some plant extracts.

**Keywords :** Langerhans cell, stress, CD39, chemokine

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