# A role for transforming growth factor-beta1 in maintaining the differentiated state of Langerhans cells in human epidermis

**Laura Pieri, Lola Domenici and Paolo Romagnoli**

Department of Anatomy, Histology and Forensic Medicine of the University of Florence, Florence, Italy

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SUMMARY

Since during the generation of dendritic cells transforming growth factor (TGF)-beta1 is required to generate specifically Langerhans cells, we have addressed whether TGF-beta1 also affects the number and immunophenotype of Langerhans cells within the epidermis. Isolated human epidermal sheets were cultured as follows: serum free; with serum; serum free with TGF-beta1; with serum plus anti-TGF-beta1; with serum plus an irrelevant antibody of the same isotype as anti-TGF-beta1. The expression of Langerhans cell antigens was analyzed by immunofluorescence and the preservation of epidermal structure and the expression of E-cadherin by electron microscopy. The number, surface area and perimeter length of Langerhans cells were measured and the results subjected to analysis of variance. Independent of serum, the architecture of the isolated epidermis was well preserved and E-cadherin was expressed for at least 48 h. In cultures without serum, Langerhans cells appeared well preserved when stained for MHC-II antigens. On the contrary, their number, surface area and perimeter length were significantly decreased upon labeling for CD1a and langerin, indicating altered expression and distribution of these differentiation specific antigens. These alterations were not accompanied by the expression of antigens of mature dendritic cells and were almost entirely prevented by serum. TGF-beta1, 1.0 ng/mL, had similar effects as serum on CD1a and langerin expression and distribution within cells, whereas anti-TGF-beta1 antibodies neutralized the effect of serum. The results indicate that Langerhans cells depend on soluble factors for the maintenance of the differentiated state within epidermis and that TGF-beta1 is a major one of such factors.

## INTRODUCTION

Langerhans cells (LC) are the antigen presenting, dendritic cells of the immune system within epidermis. They are in the differentiation stage of so-called immature dendritic cells, very efficient in the uptake and processing of antigens but poor in