GATA-3 expression in normal and pathological human skin conditions

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Summary

The GATA family of transcription factors includes a family of zinc finger domain-containing proteins with six members (GATA-1-6) that interact with a common deoxyribonucleic acid (DNA)-binding sequence. GATA-3 plays a central role in regulating Th1 and Th2 cell differentiation. In particular, GATA-3 is essential for the expression of a number of Th2 cell-specific cytokines such as interleukin (IL)-4, IL-5 and IL-13 and in inhibiting the Th1 cytokines. Furthermore, a recent investigation has demonstrated that this transcription factor is essential for stem cell lineage determination in skin. Up to now, the expression of GATA-3 has not yet been studied in pathological skin conditions. In this study, we examined the in situ expression of GATA-3 in normal human skin and in a large series of inflammatory and neoplastic skin conditions by means of immunohistochemistry.

Introduction

The GATA family of transcription factors includes a family of zinc finger domain-containing proteins with six members (GATA-1-6) that interact with a common deoxyribonucleic acid (DNA)-binding sequence. GATA-3 plays a central role in regulating Th1 and Th2 cell differentiation. In particular, GATA-3 is essential for the expression of a number of Th2 cell-specific cytokines such as interleukin (IL)-4, IL-5 and IL-13 and in inhibiting the Th1 cytokines. Furthermore, a recent investigation has demonstrated that this transcription factor is essential for stem cell lineage determination in skin. Up to now, the expression of GATA-3 has not yet been studied in pathological skin conditions. In this study, we examined the in situ expression of GATA-3 in normal human skin and in a large series of inflammatory and neoplastic skin conditions by means of immunohistochemistry.
Material and methods

The study included tissue samples of normal human skin and 37 cases of pathological skin conditions (Table 1). All tissue samples had been obtained for diagnostic purposes. Tissues were snap-frozen in liquid nitrogen and stored at -80°C. Detection of GATA-3 was performed on frozen sections from reactive and neoplastic skin conditions using an anti-GATA monoclonal antibody (HG3-31, sc-268, Santa Cruz Biotechnology, USA). The following mAbs were also used in the study: CD3 (clone UCHT1, Dako, Glostrup, Denmark), CD4 (clone MT310, Dako), CD5 (clone DK23, Dako), CD7 (clone DK24, Dako), CD8 (clone DK25, Dako), and CD19 (clone HD37, Dako). Air-dried, acetone fixed frozen sections were incubated overnight with the mAbs and, after washing, processed with an alkaline phosphatase anti-alkaline phosphatase (APAAP)-based detection system (EnVision G/2 System/AP, Dako, Glostrup, Denmark). Sections were counterstained for 5 min with Mayer’s hematoxylin. Negative controls were performed by omitting the primary mAb on samples or by the replacement of the primary antibody with another irrelevant mAb of identical isotype.

Results and discussion

We evaluated the expression of GATA-3 in normal human skin and in a number of skin tissues affected by established inflammatory and neoplastic conditions. In normal human skin GATA-3 expression was inconsistently observed only in correspondence of the matrix of the hair follicle (Figure 1). In none of the 37 pathological skin conditions investigated expression of GATA-3 was observed. The finding of GATA-3 expression in the matrix of the hair follicle is consistent with a study by Kaufman CK et al. (14), which has shown that this transcription factor is essential for stem cell lineage determination in skin and for directing epidermal stem cells to become inner root sheath cells. Furthermore, GATA-3-null embryos show aberrations in hair follicle morphogenesis that include not only structural defects in the inner root sheath and in the hair shaft, but also molecular defects in cell lineage determination (14). Although GATA-3 has been recently described to be localized in the spinous layer of the interfollicular epidermis (16), in our study we didn’t find the expression of GATA-3 in the spinous layer probably because of the different technique used. However, the role of GATA-3 in epidermis, as well as its epidermal target genes, has not been fully established so far. It has been shown that during keratinocytes differentiation there is a significant accumulation of GATA-3 protein and a parallel increase for TAP63 and keratin 10 proteins (17). Keratin 10 has been implicated in the control of basal cell proliferation through transmission of a signal from the suprabasal to the basal compartment of the epidermis (18), whereas Tap63 has a key role for both initiation of epithelial stratification and inhibition of terminal differentiation (19, 20). However, in our investigation, we could not confirm expression of GATA-3 by epidermal keratinocytes.

In this study, we have demonstrated that none of the T-cell mediated inflammatory and neoplastic skin diseases expressed the GATA-3 protein. These findings suggest that this molecule may not have a pivotal role in the pathophysiology of these conditions, although a regulatory role of in cutaneous T-cell activation may not be excluded. In fact, it is plausible that GATA-3 could be only transiently expressed on mature T cells and this may determine the absence of reactivity of T-cells with the anti-GATA 3 mAb. A further possibility is that GATA-3 in skin T-lymphocytes is generally downregulated and expressed below the detectable threshold for our immunohistochemical approach.

Table 1 - Tissues investigated in this study.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of cases</th>
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<tbody>
<tr>
<td>Atopic dermatitis</td>
<td>3</td>
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<tr>
<td>Chronic cutaneous GVHD</td>
<td>1</td>
</tr>
<tr>
<td>Contact dermatitis</td>
<td>9</td>
</tr>
<tr>
<td>Cutaneous B-cell lymphoma</td>
<td>4</td>
</tr>
<tr>
<td>Cutaneous T-cell lymphoma CD30+</td>
<td>2</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>4</td>
</tr>
<tr>
<td>Mycosis fungoides</td>
<td>5</td>
</tr>
<tr>
<td>Parapsoriasis</td>
<td>2</td>
</tr>
<tr>
<td>Pityriasis lichenoides et varioliformis acuta</td>
<td>1</td>
</tr>
<tr>
<td>Polymorphous drug eruption</td>
<td>1</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>5</td>
</tr>
</tbody>
</table>
References