Blistering and inflammation in the skin of transgenic mice expressing human IKKα only in the nucleus of keratinocytes.

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Abstract

IKKα is part of the cytoplasmic kinase IκB complex (IKK) necessary for the activation of the NF-κB transcription factor in the canonical and alternative pathways, which regulates a large number of genes involved in different processes of the immune and inflammatory response, cell proliferation and apoptosis. IKKα exerts a wide variety of functions that depends on its nuclear or citoplasmatic localization in cells being one of them the control of the terminal differentiation of the epidermis that exerts in the nucleus of keratinocytes independently of its kinase activity. According to this function, it is likely that disturbances in the levels of expression or subcellular localization of IKKα leads to the development of skin diseases. However, this is an underexplored subject. Recently, we have analyzed transgenic mice expressing human IKKα under the control of the keratin 5 (K5) promoter in the nucleus of keratinocytes both in the presence and absence of endogenous IKKα (K5-N-hIKKα and mIKKα-/-/N-hIKKa mice, respectively). The histopathological examination of our two mouse models showed regions of epidermal atrophy and an exacerbated epidermal differentiation; in addition, other changes detected in the skin of IKKα include the appearance of areas of inflammation and sporadic foci of dermoepidermal separation or intraepidermal rupture. Immunohistochemical analysis showed defects on the expression of Desmoglein 3, K5 and collagen XVII in the skin of transgenic mice, as well as foci of CD45 positive staining indicating the presence of inflammatory cells. Thus, our data suggest that the dysregulation of IKKα signaling could be involved in the appearance of inflammatory blistered cutaneous diseases.

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