Neuronatin is related to keratinocyte differentiation by up-regulating involucrin.

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Abstract

BACKGROUND: Neuronatin (Nnat), which is a neuronal developmental and differentiation molecule, is expressed in the endoplasmic reticulum of non-neuronal cells and is involved in insulin secretion from pancreatic β-cells by plausibly modulating their intracellular calcium concentration. However, the role of Nnat in keratinocyte differentiation remains unclear.

OBJECTIVE: To unveil a possible integration of Nnat in controlling the keratinocyte differentiation markers such as involucrin, cytokeratin1, filaggrin, loricrin and S100A7.

METHODS: Immunohistological staining was done using psoriasis, chronic eczema, lichen planus and normal skin. Immunofluorescence staining, Western blotting and semi-quantitative real-time PCR were performed for detecting Nnat, involucrin, cytokeratin1, filaggrin, loricrin and S100A7 using human keratinocytes with or without Nnat gene transfection. Small interference RNA was applied to knockdown the Nnat gene expression.

RESULTS: Nnat existed in normal human epidermis and cultured keratinocytes. In the hyperplastic epidermis of psoriasis, chronic eczema and lichen planus, over-expression of Nnat was evident along with involucrin and cytokeratin1 expression. Coordinate up-regulation of Nnat and involucrin, but not cytokeratin1, was demonstrated in cultured keratinocytes under differentiation stimuli such as extracellular calcium elevation, exposure to phorbol myristate acetate, and increased cell density. Transfection of small intereference RNA for Nnat decreased the mRNA levels of Nnat and involucrin, but not of cytokeratin1. Furthermore, a gene transfection assay showed increased involucrin expression in the Nnat-transfected keratinocytes than in mock-transfected counterparts, without any appreciable influence on cytokeratin1, filaggrin, loricrin and S100A7 expression.

CONCLUSION: These data indicate that Nnat is related to keratinocyte differentiation by up-regulating involucrin expression.

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KEYWORDS: Cytokeratin1, Filaggrin, Involucrin, Keratinocyte, Neuronatin

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