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| **Clinical manifestation, skin barrier properties, cytokines and gene expression in Korean X-linked recessive patients diagnosed with FISH analysis** |
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| The disruption of skin barrier is directly or indirectly associated with various skin diseases. However, the molecular mechanism to regulate skin barrier homeostasis has not been fully elucidated. Here we report that a novel protein, MAP17, regulates filaggrin gene transcription in normal human keratinocytes (NHK), discovered from bioinformatics studies with public microarray databases like the NCBI Gene Expression Omnibus (GEO). In order to understand molecular mechanisms of abnormal skin barrier development, we meta-analyzed the public microarray data for skin diseases like atopic dermatitis, psoriasis, eczema, and acne. However, meta-analyses of public microarray databases are limited by the impossibility to verify the microarray results by independent measurements using identical or similar clinical samples. In this study, we compared the transcription profile of epidermal differentiation marker genes with that of the target genes identified in the meta-analysis. Because each dermatological disease has its unique CD4 positive T helper (Th) cell profile, we postulated that the effects of Th cell cytokines on NHK may be useful to the confirmation of meta-analysis results. We confirmed that the mRNA expression profiles in response to Th1, Th2 and Th17 cell cytokines in NHK may provide an alternative approach to validate the candidate genes identified in the meta-analyses of the four dermatological diseases. Of the candidate target genes from the meta-analysis, we found that MAP17 was significantly up-regulated in response to interferon gamma, interleukin 4 (IL-4), IL-6, IL-17A, or IL-22, in NHK. In an attempt to evaluate whether MAP17 regulates the expression of cornified envelope-associated genes at the 1q21 locus such as filaggrin, loricrin, and involucrin, we found that the over-expression of MAP17 in HaCaT keratinocytes significantly decreased the expression of filaggrin. Taken together, the Th cell cytokine-induced up-regulation of MAP17 expression may be linked to the down-regulation of filaggrin in NHK, which may be associated with the abnormal epidermal differentiation observed during skin aging and in the dermatologic diseases. Therefore, the bioinformatics to meta-analyze public microarray databases will provide open opportunities to advance knowledge on human skin biology and diseases.(: 350단어이내 영문작성) |
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| **Keywords :** Skin barrier, MAP17, Bioinformatics, Microarray, Meta-analysis **(5개이하 반드시)** |

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