Plaque psoriasis is a common chronic inflammatory skin disease. To date, most efficient antipsoriatic drugs are biologicals that inhibit some key cytokines in the pathogenetic network of psoriasis. Interleukin (IL) 36α (gene symbol IL36A), IL-36β (IL36B), IL-36γ (IL36G), IL-36Ra (IL36RN), IL-37 (IL37) and IL-38 (IL1F10) are new members of the IL-1 cytokine family. We have recently conducted RNA sequencing of psoriatic lesional, nonlesional and control skin [1]. Our whole transcriptome analysis revealed that most of these cytokines were significantly deregulated in psoriatic skin. Herein, we report our results from RNA sequencing regarding the expression of IL-36-38 in more detailed way. Additionally, we utilized immunohistochemistry to provide further evidence of the expression of IL-36-38 in more detailed way. Furthermore, IL-36 cytokines themselves can induce the expression of proinflammatory TNF-α, IL-6 and IL-8, and IL-36 itself in KC [2]. Also, it has been observed that IL-36 cytokines are rather skin specific, which makes them attractive potential treatment target. For instance, it was established by Tortola et al. that IL-36 receptor (IL-36R) deficient mice were protected from imiquimod-induced expansion of dermal IL-17 producing T-cells and psoriasiform dermatitis, whereas IL-36R antagonist (IL-36RN) deficient mice exhibited aggravated pathology [4]. In another experiment blockade of IL-36R reduced epidermal hyperplasia and other histopathologic changes associated with psoriasis in human psoriatic lesional skin transplanted onto immunodeficient mice and the results were even comparable with the effects of etanercept [5].

With regard to IL36RN, which encodes an antagonist to proinflammatory IL-36 cytokines, the likeliest explanation for similar expression profile could be a negative feedback. Interestingly, different studies have found association between IL36RN mutation leading to loss of protein function and generalized pustular psoriasis [6,7].

The expression of IL37 was clearly different from genes encoding IL-36 cytokines. The expression of IL37 was decreased 0.8 times ($P = 0.003$, FDR = 0.01) in psoriatic lesional skin compared with controls and 1.5 times ($P = 3.23 	imes 10^{-8}$, FDR = $7.26 	imes 10^{-7}$) when compared with psoriatic nonlesional skin (Fig. 1c). It was the only cytokine of those under investigation that was underexpressed in psoriatic lesional skin. It is consistent with the recent results by Li et al. [8] who also described downregulation of IL37 in lesional psoriasis by RNA sequencing. This is not a surprising finding because of the anti-inflammatory nature of IL-37. IL-37 is less studied in psoriasis in comparison with IL-36 cytokines but in very recent study with two transgenic mouse models of psoriasis it was observed that IL-37 inhibited the overexpression of CXCL8, IL-6 and S100A7 [9]. Although IL-37 is not as skin specific as IL-36 cytokines, it might be still another promising novel treatment target for psoriasis.

In contrast to IL-36 cytokines and IL-37, there were no statistically important differences in the expression of
IL-38 encoding IL1F10 between study groups (Fig. 1f). There is even less known about the exact role of IL-38. As for psoriasis, the only link we could find in the literature was between single nucleotide polymorphism in the region encoding IL-38 and susceptibility to psoriatic arthritis [10].

Despite there is growing evidence about the connections between IL-36 cytokines and psoriasis, it seems that their role is...
still somewhat underestimated so far. With the present work we highlight the pivotal role of IL-36 cytokines in plaque psoriasis and among the first suggest that also IL-37 but not IL-38 is involved in psoriatic skin inflammation.

Conflict of interest

The authors have no conflict of interest to declare.

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References


Skin aging is clinically characterized by the wrinkle formation associated with damage of dermal extracellular matrix (ECM) [1]. Recent study has indicated that expression of ABO blood group antigens (ABH antigens) are reduced in the sun exposed skin, suggesting that ABH antigens may be implicated in photoaging process [2]. Hence, the present study was aimed to investigate the possible anti-aging potential of ABH antigen synthesis-increasing materials on ECM protein production in human skin, which are mixtures of natural plant extracts (Camellia sinensis (Green tea) leaf extract, Polygonum cuspidatum root extract; Biospectrum, Seongnam, Republic of Korea; Ginkgo biloba leaf extract, Cynara scolymus (Artichoke) leaf extract, Selaginella tamariscina extract; kindly gifted from Amorepacific R&D Institute, Yongin, Republic of Korea) and ABH antigen-composing monosaccharides (D-Glucose, D-Galactose, L-Fucose, N-acetyl-D-galactosamine, N-acetyl-D-galactosamine; Sigma–Aldrich, St. Louis, MO), increasing ABH antigen expression in HaCaT cells and human skin (Suppl. Figs. S1 and S2), by immunohistochemical determination of ECM proteins.

Letter to the Editor

Beneficial effects of blood group antigen synthesis-increasing natural plant extracts and monosaccharides on extracellular matrix protein production in vivo

Keywords

ECM protein
Natural plant extract
Monosaccharides
Anti-aging
Blood group antigen

Abbreviations: ECM, extracellular matrix.