Poster Presentations

P1
Effect of Thioredoxin Reductase 1 on Glucocorticoid Receptor Activity in Human Outer Root Sheath Cells
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Alopecia areata (AA) is a common disease of patchy hair loss on the scalp that can progress to cover the entire scalp and eventually the entire body. Intraleisional injection of corticosteroids is the first-line therapy for adult patients, and it is believed that the effect of glucocorticoid is mediated through an immunosuppressive mechanism primarily. Although it is a very powerful treatment for AA, some patients do not respond to glucocorticoid treatment effectively. To delineate the molecular mechanism underlying glucocorticoid insensitivity, we examined the expression of glucocorticoid receptor (GR) and thioredoxin reductase 1 (TrxR1) in AA patients. In some cases of glucocorticoid resistant AA, the expression of TrxR1 was significantly decreased in outer root sheath (ORS). We then investigated the effect of TrxR1 on GR activity using recombinant adenosviruses. The ORS cells were transduced with TrxR1- and GR-expressing adenosviruses together with reporter virus. The results showed that TrxR1 significantly increased GR activity. Next, we determined the effect of TrxR1 on endogenous GR activity of ORS cells. As anticipated, overexpression of TrxR1 markedly increased endogenous GR activity. These results suggest that decreased TrxR1 may lead to a lower responsivity to glucocorticoid treatment via a decrease in GR activity.

P2
T-Flavanone Suppresses BMP-4 Production in Dermal Papilla Cells
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The results from our recent study suggest that there are multiple pathways through which t-flavanone stimulates hair growth. One such pathway previously reported was t-flavanone fs suppression of TGF-b2 activation on keratinocytes (10th EHRS, Barcelona, 2003). In this study, we identified another pathway by focusing on dermal papilla cells, which secrete many hair growth-related molecules. We found that conditioned medium collected from dermal papilla cells that had been treated with t-flavanone induced keratinocyte proliferation. Gene Chip and RT-PCR analysis revealed that t-flavanone decreased the mRNA expression of BMP-4 in a dose-dependent manner. The expression and secretion of BMP-4 protein also decreased in a similar manner. Furthermore, the and secretion of BMP-4 protein also decreased in a similar manner. Furthermore, the addition of recombinant BMP-4 to keratinocytes suppressed their proliferation. In contrast, the addition of a BMP-4 neutralizing antibody into an untreated dermal papilla cell-derived conditioned medium promoted keratinocyte proliferation in a dose-dependent manner. These results indicate that t-flavanone stimulates hair growth by suppressing BMP-4 in dermal papilla cells as well as by suppressing activation of TGF-b2 on keratinocytes.

P3
Induction of Versican by Ascorbic Acid 2-Phosphate in Dermal Papilla Cells
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We have recently reported that L-ascorbic acid 2-phosphate magnesium salt (Asc 2-P), a derivative of L-ascorbic acid (Vitamin C), promotes the elongation of hair shafts in hair follicles in culture and induces early conversion from a telogen phase to an anagen phase in mice, demonstrating that Asc 2-P affects hair growth and cycling. Here, we investigated whether Asc 2-P regulates expression of versican, which is thought to play an important role in anagen induction and maintenance of normal hair growth, in cultured dermal papilla cells and in dermal papillae of isolated hair follicles in culture. Hair biopsy specimens were obtained from the non-balding occipital scalp region of patients with androgenic alopecia. Dermal papilla cells of the 2–3 passage were used in this study. Immunohistochemical staining of versican was performed with rabbit polyclonal antibody recognizing versican V0 and V1 isoforms. We observed that isoforms of versican were up-regulated in dermal papilla cells by Asc 2-P treatment. Immunohistochemical staining also revealed increased expression of versican, at least V0 and V1, in dermal papilla of isolated hair follicles treated with Asc 2-P. LY294002, a pharmacological inhibitor of PI3K, significantly attenuated Asc 2-P-induced versican expression. We also observed that Asc 2-P activates/phosphorylates PKB, a downstream effector of PI3K, and that LY294002 attenuates Asc 2-P-mediated phosphorylation of PKB. In addition, we observed that nuclear β-catenin is increased by Asc 2-P in a dose-dependent manner and LY294002 reduces nuclear accumulation of β-catenin. This study demonstrates that Asc 2-P induces versican expression via PI3K signaling and causes nuclear β-catenin accumulation in dermal papilla cells. Since versican is thought to play an important role in anagen induction and maintenance of the normal hair growth, it would be worthwhile to evaluate vitamin C or its derivatives as a novel approach for treatment and prevention of hair loss.