Synopsis of Original Research Paper

The role of 11β-hydroxysteroid dehydrogenase type 1 in skin aging

Mika Terao

Department of Dermatology Osaka University Graduate School of Medicine

Glucocorticoids (GCs) are one of the most effective anti-inflammatory drugs to treat acute and chronic inflammatory diseases. However several studies show that GCs alter collagen metabolism in the skin and induce skin atrophy. Cortisol is the endogenous GC that is released in response to various stressors. Over the last decade, extraadrenal cortisol production in various tissues is reported. Skin is also known to synthesize cortisol though *de novo* pathway and through activating enzyme. 11β-hydroxysteroid dehydrogenase 1 (11β-HSD1) is the enzyme that catalyzes the conversion of hormonally inactive cortisone into active cortisol in cells. We previously found that 11β-HSD1 is negatively regulating proliferation of keratinocytes. To know the function of 11β-HSD1 in dermal fibroblast and collagen metabolisum, the effect of selective 11β-HSD1 inhibitor was studied in mouse tissues and dermal fibroblasts. The expression of 11β-HSD1 increased with age in mouse skin. Subcutaneous injection of selective 11β-HSD1 inhibitor increased dermal thickness, and collagen content of the mouse skin. Proliferation of dermal fibroblasts significantly enhanced in cells derived from 11β-HSD1 knockout mice compared with cells derived from wildtype mice. Taken together, these data suggest that 11β-HSD1 is involved in collagen metabolism in the skin possibly by decreasing the proliferation of dermal fibroblasts. Our findings suggest that 11β-HSD1 inhibition may reverse the decreased collagen content observed in intrinsically and extrinsically aged skin and in skin atrophy that is induced by GC treatment.