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CLAUDIN-5 DEFICIENCY INDUCED BY MICRORNA-224-5P CONTRIBUTED TO DEFECTIVE PERMEABILITY BARRIER IN SENSITIVE SKIN

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Introduction: Sensitive skin is a skin condition that is hypersensitive to various external stimuli. Although the pathogenic role of defective epidermal permeability barrier is appreciated, the underline molecular mechanisms remain unknown.

Objective:The purpose of this study is to explore the expression and regulation of claudin-5 in the pathogenesis of sensitive skin.

Materials and Methods: RNA-seq analyses were used to identify gene differentially expressed in sensitive skin and normal skin. The results were validated using quantitative real-time polymerase chain reaction and immunofluorescence. Changes in ultrastructure of epidermal intercellular junction in sensitive skin was assessed using electron microscopy. The link between microRNA-224-5p and CLDN5 was determined using quantitative real-time polymerase chain reaction, Western Blotting, Luciferase reporter gene assay and rescue test in vitro. To investigate the impact of CLDN5 deficiency on the skin barrier, CLDN5 was knocked down using small interfering RNA (siRNA) in keratinocytes and organotypic cultures in vitro.

Results: In comparison to normal skin, sensitive skin displayed a reduction in CLDN5 expression and elevation in microRNA-224-5p expression. Electron microscopy revealed that the intercellular junction was disrupted. MicroRNA-224-5p downregulated CLDN5 expression in keratinocytes, leading to an increase in paracellular permeability in organotypic cultures. MicroRNA-224-5p directly interacted with the 3`UTR of CLDN5 in keratinocytes.

Conclusion: MicroRNA224-5p induced claudin-5 deficiency results in a defective permeability barrier, suggesting that microRNA-224-5p could be a potential target for the treatment of sensitive skin.