Synopsis of Original Research Paper

# Molecular mechanisms for collapse of dermoepidermal junction caused by XVII collagen abnormality.

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Mutations in the gene encoding type XVII collagen have been shown to cause generalized atrophic benign epidermolysis bullosa (GABEB), which is characterized by generalized blistering with skin atrophy, enamel hypoplasia diffuse alopecia and nail dystrophy. To further understand the role of type XVII collagen in the integument, we examined two unrelated GABEB families and also four patients with amelogenesis imperfecta (AI), which comprises a clinically and genetically diverse group of conditions affecting the development of dental enamel. Ultrastructural examination of the GABEB patients' skin revealed tissue separation in the lamina lucida and immunohistochemical analyses showed no or little expression of type XVII collagen in the epidermal basement membrane zone. Mutation analysis of the *COL17A1* gene encoding type XVII collagen revealed that patient 1 was compound heterozygous for a deletion and a nonsense mutation (1285delA and Q1387X) and that the patient 2 carried homozygous deletion mutations 4335delC. The developmental mechanism of enamel hypoplasia in GABEB has yet to be elucidated. To understand the possible *COL17A1* function in enamel formation, we investigated whether mutations exist within the *COL17A1* gene in the patients with AI. However, no significant nucleotide changes were found in the gene, suggesting no significant relation between collagen XVII and enamel disease. Further analysis of GABEB patients and *COL17A1* function is required to understand precise mechanisms whereby these mutations can induce multiple symptoms in the integument.