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Phenotype-Genotype Correlations in Patients with Epidermolysis Bullosa with PLEC Mutations

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PHENOTYPE-GENOTYPE CORRELATIONS IN PATIENTS WITH EPIDERMOLYSIS BULLOSA WITH PLEC MUTATIONS

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Epidermolysis bullosa (EB) is a heterogeneous group of genetic disorders characterized by blistering skin and mucous membranes. Mutations of the protein plectin, encoded by PLEC, cause autosomal recessive EB simplex with muscular dystrophy (EBS-MD) and EB simplex with pyloric atresia (EBS-PA). Until now, no clear genotype-phenotype correlation has been identified from the positions of mutations in the PLEC gene. How do ten distinct families with PLEC mutations manifesting as various EB disorders compare with regard to gene mutations? The hypothesis is that clinical manifestations of EB will be more extreme in patients with more severe gene mutations.

The design of this study is a case series following ten distinct families in Iran with PLEC mutations. The clinical data collection was done by the patients' physicians in Iran. The mutation detection and data analysis were done at Jefferson's Department of Dermatology. Genotype severity was measured by exon and type of mutation. Phenotype severity was measured by both cutaneous and extracutaneous manifestations.

The majority of EBS-MD PLEC mutations were within exon 31, whereas the EBS-PA PLEC mutation was outside exon 31. However, there was no clear genotype phenotype correlation. Patients with EBS and EBS-MD had nonsense, missense and frameshift mutations, whereas the EBS-PA patient had a splicing mutation.

Although the inquiry question was not answered, other measures of phenotype severity, such as serum markers, electromyography (EMG), and skeletal muscle biopsy staining, can be correlated with genotype severity in future work. Using a relatively large and rare cohort of patients, each patient can be analyzed to better understand the pathophysiology of EB and enhance its diagnostic and treatment methods.