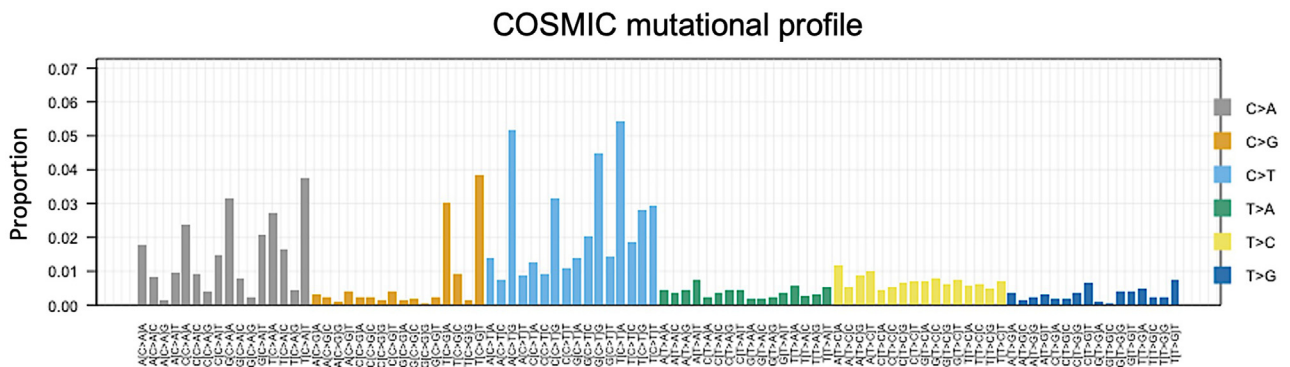


Supplementary Figure S1. Full list of enriched pathways from KEGG analysis. KEGG, Kyoto Encyclopedia of Genes and Genomes.



Supplementary Figure S2. COSMIC mutational profile of somatic mutations from RDEB-proband SCC compared with those from the skin using the conventional 96 mutation type classification. The proportion of single-nucleotide substitutions is shown on the y-axis. A total of 96 trinucleotide categories depicting 6 substitution subtypes—C>A, C>G, C>T, T>A, T>C, T>G—and the nucleotides at the 5' and 3'-ends of the substitutions are shown on the x-axis. COSMIC, Catalogue of Somatic Mutations in Cancer; RDEB, recessive dystrophic epidermolysis bullosa; SCC, squamous cell carcinoma.

Supplementary Table S1. Calculation of Mutational Burden for the Proband's Blood, Skin, and SCC

Tumor Sample	Normal Sample	Total somatic Variants	Nonsynonymous Somatic Variants	Nonsynonymous TMB
SCC	Blood	9867	759	0.263 per Mbp
SCC	Skin	10,085	749	0.260 per Mbp
Skin	Blood	667	76	0.027 per Mbp

Abbreviations: SCC, squamous cell carcinoma; TMB, tumor mutational burden.

Total somatic variant counts were obtained using the Strelka analysis algorithm. The number of nonsynonymous variants were identified from all possible combinations and divided by the total coverage of 2884.957 Mbp to calculate the TMB values.