Appendix S1.

SUPPLEMENTARY METHODS

Patient samples, immunofluorescence, ultrastructural and molecular analyses

Skin biopsies and blood samples were obtained after informed consent, with the approval of the ethics committees of each participating institution and in accordance with Declaration of Helsinki guidelines.

Skin biopsies were used for immunofluorescence antigen mapping and electron microscopy examination, as described (S1). Genomic DNA purified from blood was used to scan the exome (Nextera rapid capture v.1.2, Illumina) (case 1) or the entire coding sequence of genes implicated in EB (Trusight One sequencing panel) (cases 2 and 3) on a NextSeq500 platform. Exome sequencing was designed to guarantee proper coverage (mean depth on target: 80×), and sequencing data were analysed using an in-house implemented bioinformatics pipeline (S2, S3). Variant validation and segregation analysis were performed by Sanger sequencing.

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