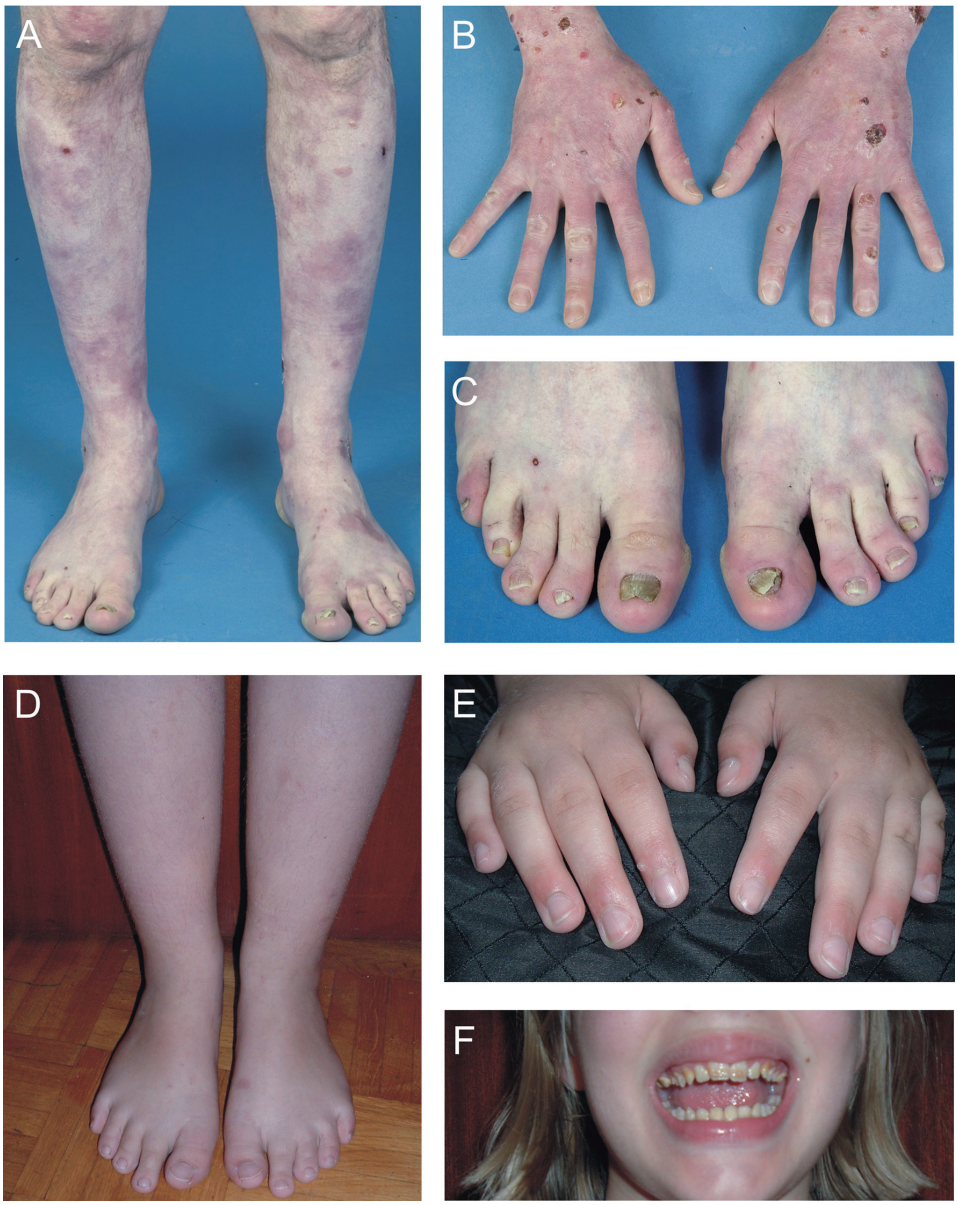
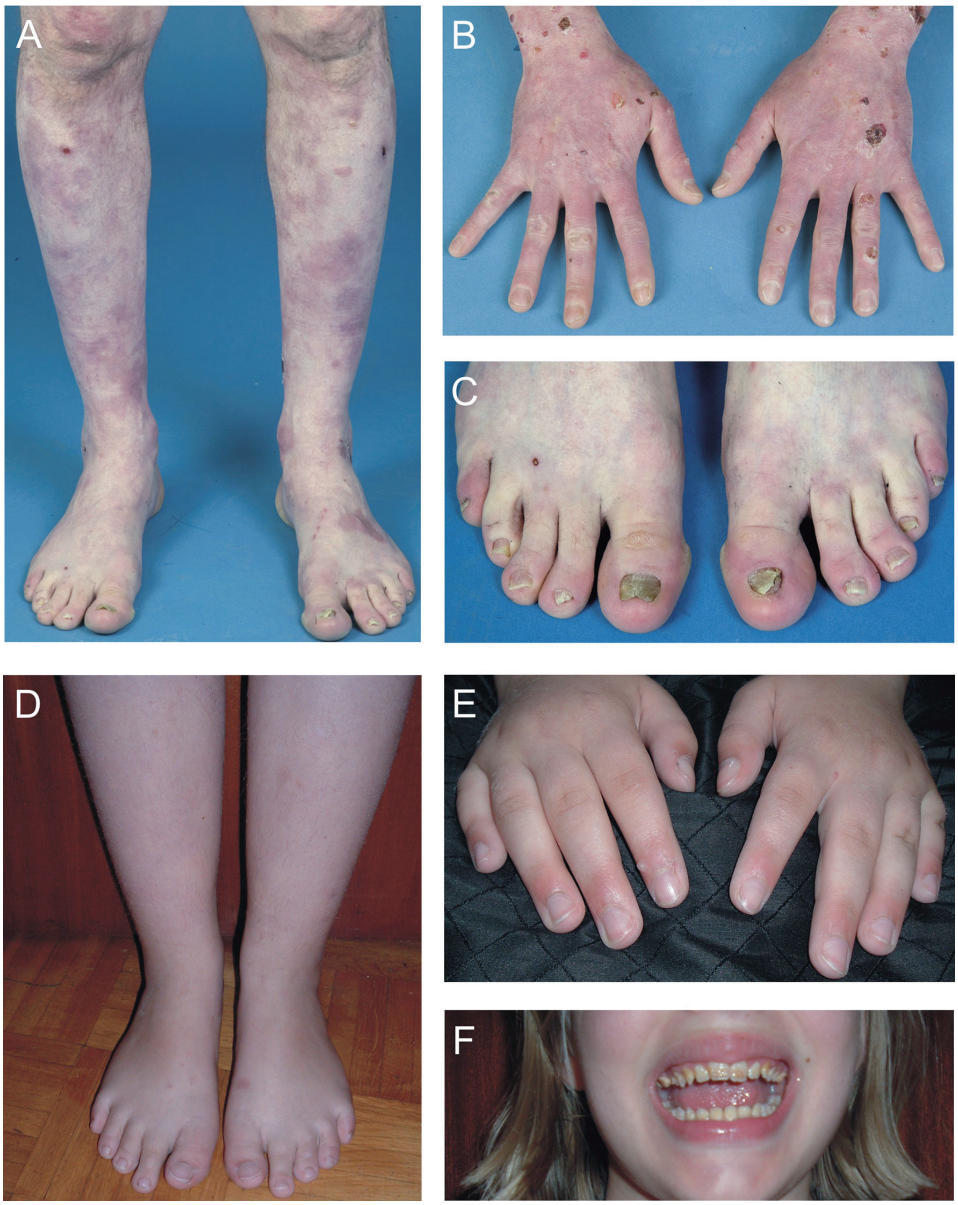


Fig. S1. Clinical phenotypes. A–C. Case 1 has generalised intermediate blisters and crusts, and dystrophic toe nails. D–F. Case 2 has only occasional acral blisters, normal nails and severe enamel defects.



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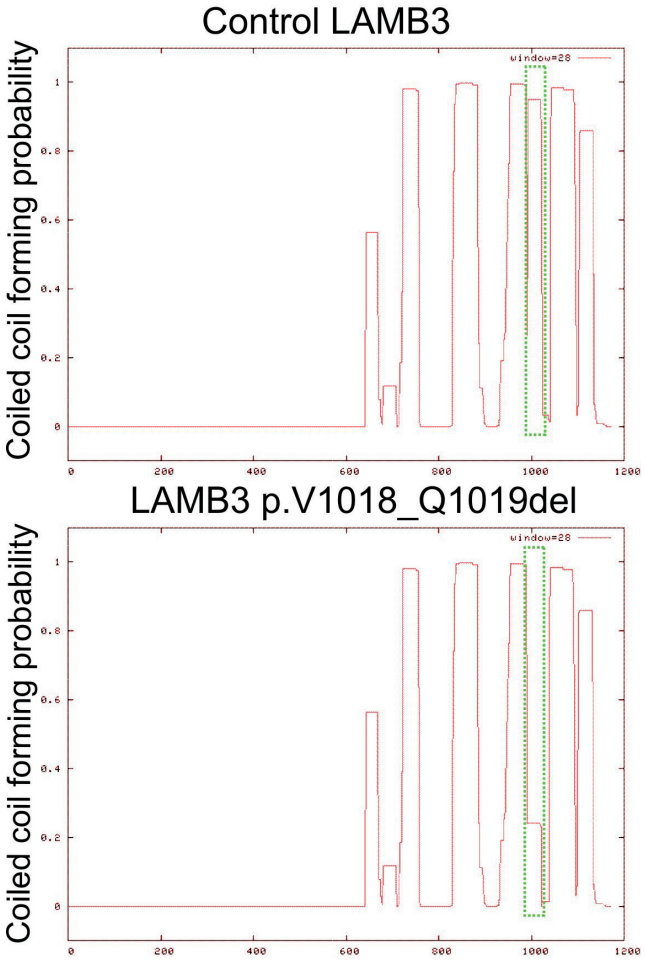

Fig. S3. Prediction of the coiled-coil structures of the laminin β3 chains. The COILS software version 2.2 (http://embnet.vital-it.ch/software/COILS_form.html) was used to assess the consequence in the coiled-coil structure due to the 2 amino acid deletion p.V1018_Q1019del in the C-terminus of the laminin β3 chain. The data revealed a significant disturbance of one coiled-coil region obtained in scanning window of 28 amino acid residues (green).

Appendix S1

MATERIALS AND METHODS

Mutation analysis of the *LAMB3* gene was performed as described before (7), after informed consent and in adherence to the Declaration of Helsinki principles. DNA was isolated from peripheral blood samples (QiAmp DNA mini kit, Qiagen, Hilden, Germany) and all *LAMB3* exons and exon/intron boundaries amplified and sequenced (ABI 7330XL DNA analyzer). The study was approved by the Ethics Committee of the University Freiburg.

For RNA extraction from case 1, 10 μm skin sections were used with the Qiagen FFPE RNA kit (Qiagen). For case 2, cultured primary keratinocytes isolated from the skin were available for total RNA isolation (Qiagen RNeasy kit, Qiagen). Reverse transcription was performed using 0.2 μg of total RNA and oligo-dT primers (Advantage RT-for-PCR Kit, Clontech, Mountain View, USA). Specific primers spanning the exons 21 and 10 were designed (http://frodo.wi.mit.edu/primer3) (Table SI). The amplicons were subcloned into the TOPO TA-cloning vector (Invitrogen, Karlsruhe, Germany), and the DNA extracted from 20 clones was sequenced with the M13-RV primer.

For immunoblotting, a snap-frozen skin sample of case 1 was crushed and lysed in a buffer containing 50 mM Tris-HCl pH 7.5, 150 mM NaCl, 0.5% sodium deoxycholate, 1% Triton X-100, 0.1% SDS and protease inhibitors. After precipitation, proteins were separated by SDS-PAGE and immunoblotted with antibodies to laminin β3 (to aa 644-930, Origene, Rockville, MD) and GAPDH (Santa Cruz Biotechnology, Heidelberg, Germany), which was used as a loading control. Keratinocytes isolated from a skin sample of case 2 were extracted with a buffer containing 0.1 M NaCl, 20 mM Tris-HCl, pH 7.4, 1% Nonidet P-40, Pefabloc and EDTA, and in parallel conditioned media were collected. Normalised amounts of the proteins and media were subjected to SDS-PAGE, and immunoblotted with antibodies to the C-terminus of laminin β3 (C-19, Santa Cruz) and GAPDH (clone 6C5, Millipore, Temecula, California).

Immunofluorescence staining of skin sections was performed using antibodies for the laminin chains: BM165 for α3 (gift from Dr. Eble, Frankfurt, Germany), 6F12 for β3 and GB3 for γ2 (both from Santa Cruz). The intensity of the immunofluorescence signals was evaluated with Image J (http://rsb.info.nih.gov/ij/).

Table SI. LAMB3 *primers for RT-PCR used in this study*

Primer	Sequence 5'-3'
20-22F	AAGATGTGGTTGGGAACCTG
20-22R	CAGCTCCTCTGCCTCTGTCT
20-22F nested	CTTCGGCTTATCCAGGACAG
20-22R nested	CAAACAGCTCCTCTGCCTCT
7-11F	CAGCGCCTACTATGCTGTGT
7-11R	GTGGTAGGGAGCACACTGGT