

Appendix S1.

## MATERIALS AND METHODS

### *Patient samples*

Following written informed consent, skin biopsies were collected from the patients and the father of patient 4. Blood samples were also obtained from the patients, their parents and the brother of patient 4. The study was conducted in compliance with the principles of the Declaration of Helsinki.

### *Immunofluorescence and electron microscopy studies*

Frozen 5 µm thick sections were obtained from skin biopsies of the patients, patient's 4 father and healthy controls and processed for indirect immunofluorescence using the following primary antibodies: monoclonal anti-human type VII collagen (LH7.2, Sigma Immunochemical, St Louis, MO, USA); monoclonal anti-human laminin-332 (clone GB3, a gift of Dr Meneguzzi, Inserm, Nice, France); monoclonal anti-human BP180 (clone 1A8C, a gift of Dr Owaribe, Nagoya University, Japan); monoclonal anti-human integrin β4, (clone 3E1, Chemicon, Merck Millipore, Billerica, MA, USA).

For electron microscopy examination, skin biopsy specimens from patients 1–4 were fixed in 2% glutaraldehyde, post-fixed in 1% osmium tetroxide, dehydrated in graded alcohols, and embedded in Epon resin. Ultrathin sections were stained with uranyl acetate and lead citrate and observed in an Omega Zeiss EM 912 transmission electron microscope.

### *Molecular analysis*

Mutational screening of *COL7A1* gene was performed by denaturing high-performance liquid chromatography (DHPLC) scanning of PCR products corresponding to the entire coding region, as described (7). Sanger sequencing of positive DHPLC amplicons was used to precisely identify the mutation. Each mutation was confirmed by a second cycle of PCR and sequencing.

### *Literature review*

A literature (English, French, Italian, German and Spanish) search was performed on PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) from 1985 to July 2015. The following key words were used: transient bullous dermolysis of the newborn, bullous dermolysis of the newborn, dermolysis and newborn, dystrophic epidermolysis bullosa and mutation, dystrophic epidermolysis bullosa and newborn. Studies describing clinical and laboratory findings of individual BDN cases were assessed. In addition, articles reporting mutational analysis of DEB case series were examined for the inclusion of BDN cases. Finally, the International Dystrophic Epidermolysis Bullosa Patient Registry was searched for BDN cases (8). Relevant information was extracted from each article and reviewed to eliminate potential duplication of case reports.

### *Statistical analysis*

The association between specific clinical features (congenital skin defects and mucosal involvement) and type of inheritance (dominant vs. recessive) was studied through the Fisher exact test. Statistical significance was set at the 0.05 level.