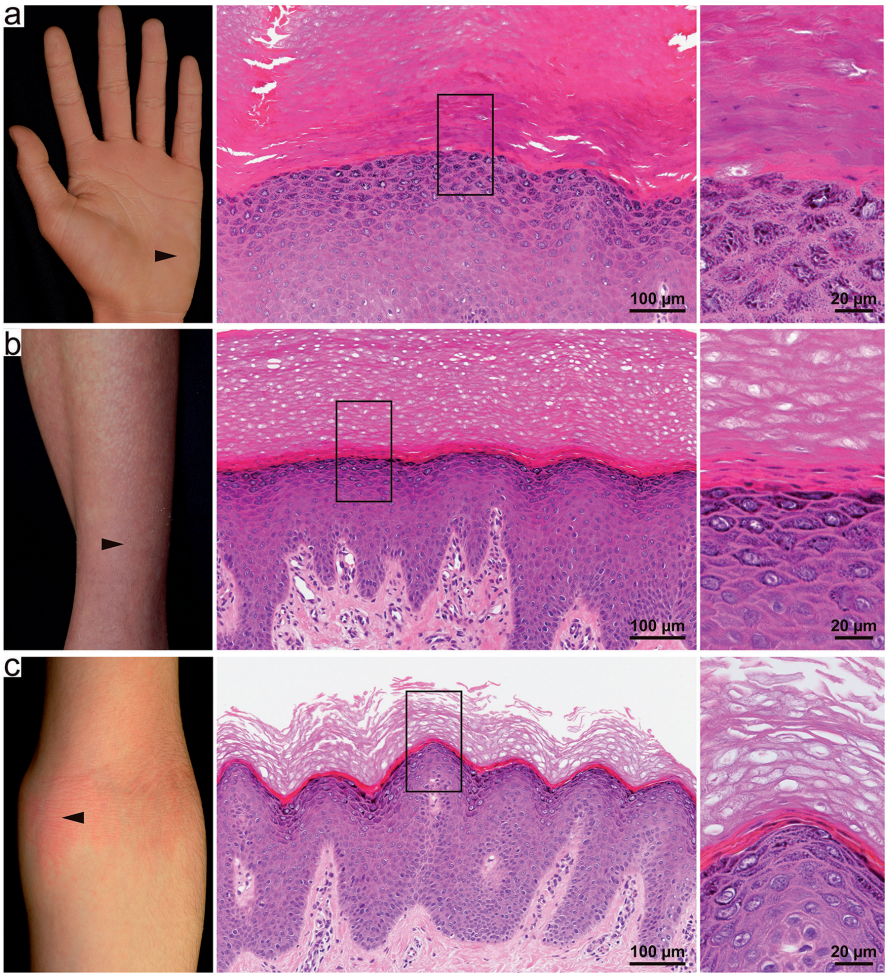

Fig. S1. Skin biopsy sites (*left-hand panels*) and histological features (*middle and right-hand panels*). Histology of lesional skin sampled from (a) the palm, (b) lower leg and (c) cubital fossa shows hyperkeratosis, acanthosis and hypergranulosis (haematoxylin and eosin, original magnification ×100). Higher magnification (*right-hand panels*) highlights parakeratosis in the lower layers of the stratum corneum (original magnification ×400). Arrowheads (*left-hand panels*) indicate the sites of skin biopsy.

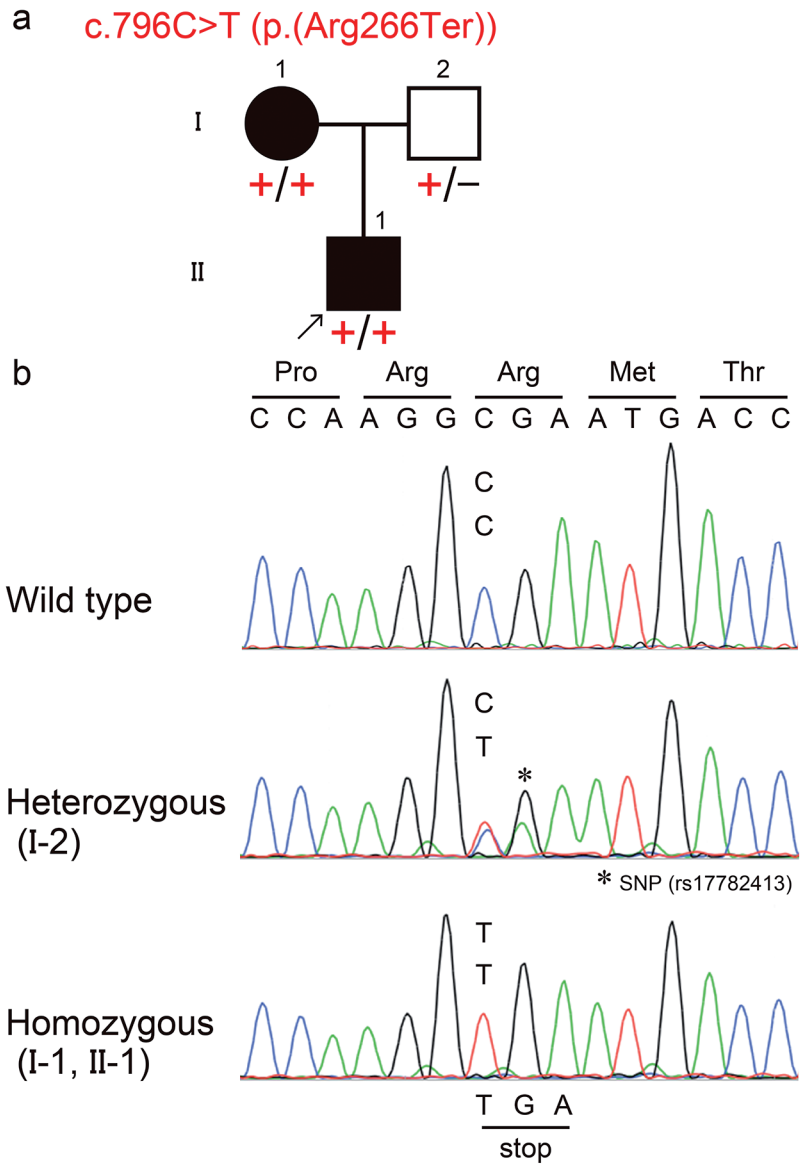

Fig. S2. Detection of *SERPINB7* mutation. (a) The pedigree of a 2-generation Japanese family with Nagashima-type palmoplantar keratosis (NPPK) shows pseudodominant inheritance. *Solid symbols*: affected individuals; *open symbols*: unaffected individuals. (b) The patient (II-1) and his mother (I-1) are homozygous for a nonsense mutation c.796C>T (p.(Arg266Ter)) in exon 8 of *SERPINB7*, whereas his father is heterozygous for the mutation. Note that the father (I-2) is also heterozygous for c.797G>A, which is a non-pathogenic single-nucleotide polymorphism (SNP) (rs17782413).

Fig. S3. Whitish spongy change upon water exposure in the affected skin. (a) The patient's palm shows the white, spongy appearance after bathing. (b, c) Similar change is observed in the affected skin on (b) the cubital fossa and (c) the lower leg after bathing.