**Supplementary figure 1** Mutation analysis of the *KRT6A* and *KRT16* genes, where the arrow represents the mutation site. (A) Heterozygous c.1393T>C (p.Tyr465His) substitution within exon 1 of *KRT6A*. (B) A novel heterozygous c.1237G>C (p.Glu413Gln) missense mutation in exon 6 of the *KRT16* gene.



**Supplementary table 1** Primer and Sequences

|  |  |  |
| --- | --- | --- |
| Gene name | Primers | Sequence 5’-3’ |
| KRT6a | Exon 1 | Forward CTGATTCCTAGTCCTGCTTCT  Reverse AAAATGCCAGGAGTACACG |
| KRT6a | Exon 2-4 | Forward CAGGAAACCGGATACCAGAC  Reverse CAGCTCCTGCAGAACAGAAG |
| KRT6a | Exon 5-6 | Forward GGGGAGAAGATGTATAGGGT  Reverse AAGTTCCAGGGGATTTTCCC |
| KRT6a | Exon 7-9 | Forward ATCAATTCTGGGCTCCTGGC  Reverse GACCGAGAGCTAGCAGACGC |
| KRT16 | Exon 1 | Forward CTGCTCACTCGCTCACCTC  Reverse GCCCAGTCTCCCTGTTTGT |
| KRT16 | Exon 2-5 | Forward CCCCTTTCTGCCTTTCAT  Reverse CTGCTGTGCTGGGTCCTT |
| KRT16 | Exon 6 | Forward GGACTCATGGGACCGTTAT  Reverse ATGGAAACAGGCAGAGGG |
| KRT16 | Exon 7-8 | Forward AGGATGCCCAGTGAGTCCCAG  Reverse AGGGGAGATAGCTGGGAACTG |
| KRT6b | Exon 1 | Forward GCTTCTCCTCCCTCTCGCCTC Reverse TGCACTCTCTGCAGAGCTGGGCTGA |
| KRT6b | Exon 2 | Forward CCTCTCGGTAAAAAAAAC Reverse ATCCTCCCATAACCATCT |
| KRT6b | Exon 3、4、5 | Forward GGACCTCAAGAACAAGTG Reverse CTAAAAGTCAGCAACCAA |
| KRT6b | Exon 6 | Forward GTTTAGTATCCACCCACC Reverse TCTGACCTGACATCTTGC |
| KRT6b | Exon 7 | Forward TTTGGTTTTTTTGCTTTG Reverse ACTGGAGACGGTGGACTG |
| KRT6b | Exon 8、9 | Forward AGCACAACTTTAAGGTG Reverse TGTAATAATACGGGAAC |
| KRT17 | Exon1 | Forward ATGGAAACAGAGGAGCAA Reverse CTAAGCCACAGCCAAACC |
| KRT17 | Exon2 | Forward GACATTTTCCCATTCT Reverse CTATTCCCTGCCTAAG |
| KRT17 | Exon3 | Forward AATAGAAGAGAAGGAGGG Reverse GAGAGTTTGAAATGGGAC |
| KRT17 | Exon4 | Forward GGTCCTTGTGGGAAGTGGGGT Reverse GGGGCACCTCCAAGACATCTGGC |
| KRT17 | Exon5、6、7 | Forward GGGCTTTGGGATGTGGGAAGC Reverse GAGGGACAGCCATCAACTCCTGG |
| *KRT17* | Exon8 | Forward TGCAGTGTGATGTCGAGGTG Reverse GGCCAGAACAAGGACACATTT |

**Supplementary table 2** Demographics and Distinguishing Clinical Symptoms among PC-K6a and PC-K16

|  |  |  |  |
| --- | --- | --- | --- |
| Mutation groups | PC-K6a  (n=364[55.7%) | PC-K16  (n=289[44.3%) | P-value |
| Demographic |  |  |  |
| Sex |  |  |  |
| Female | 198 (56.5) | 146 (54.8) | >. 05 |
| Male | 166 (43.5) | 143 (45.2) |
| Positive family history | 213 (45.7) | 228 (64.5) | <. 001 |
| Clinical symptoms |  |  |  |
| Plantar symptoms |  |  |  |
| keratoderma a | 308 (84.6) | 283 (98) | <. 001 |
| Pain b | 204 (56) | 225 (77.9) | <. 001 |
| Toenails Dystrophy |  |  |  |
| all | 336(92) | 110(38) | <. 001 |
| 7-9 | 10(3) | 37(13) |  |
| 4-6 | 6(2) | 74(26) |  |
| 1-3 | 5(1) | 57(20) |  |
| Palmar symptoms |  |  |  |
| keratoderma a | 142 (39) | 181 (62.6) | <. 001 |
| Fingernail Dystrophy |  |  |  |
| all | 321(88) | 80 (28) | <. 001 |
| 7-9 | 12(3) | 12 (4) |  |
| 4-6 | 17(5) | 37 (13) |  |
| 1-3 | 6(2) | 34 (12) |  |
| Oral leukokeratosis | 319 (88) | 98 (34) | <. 001 |
| Cyst | 218 (60) | 72 (25) | <. 001 |
| Follicular hyperkeratosis | 185 (51) | 32 (11) | <. 001 |
| Natal teeth | 16 (4) | 0 | <. 001 |

a Comparing patients reporting persistence of keratoderma as ‘‘always’’ or ‘‘sometimes’’ to those answering ‘‘seldom’’ or ‘‘never.’’  
b Comparing those reporting ‘‘very painful but no medication needed’’ or ‘‘often require medication for pain’’ to those answering ‘‘some pain’’ and ‘‘no pain.’’

All P-values calculated using χ2 test.