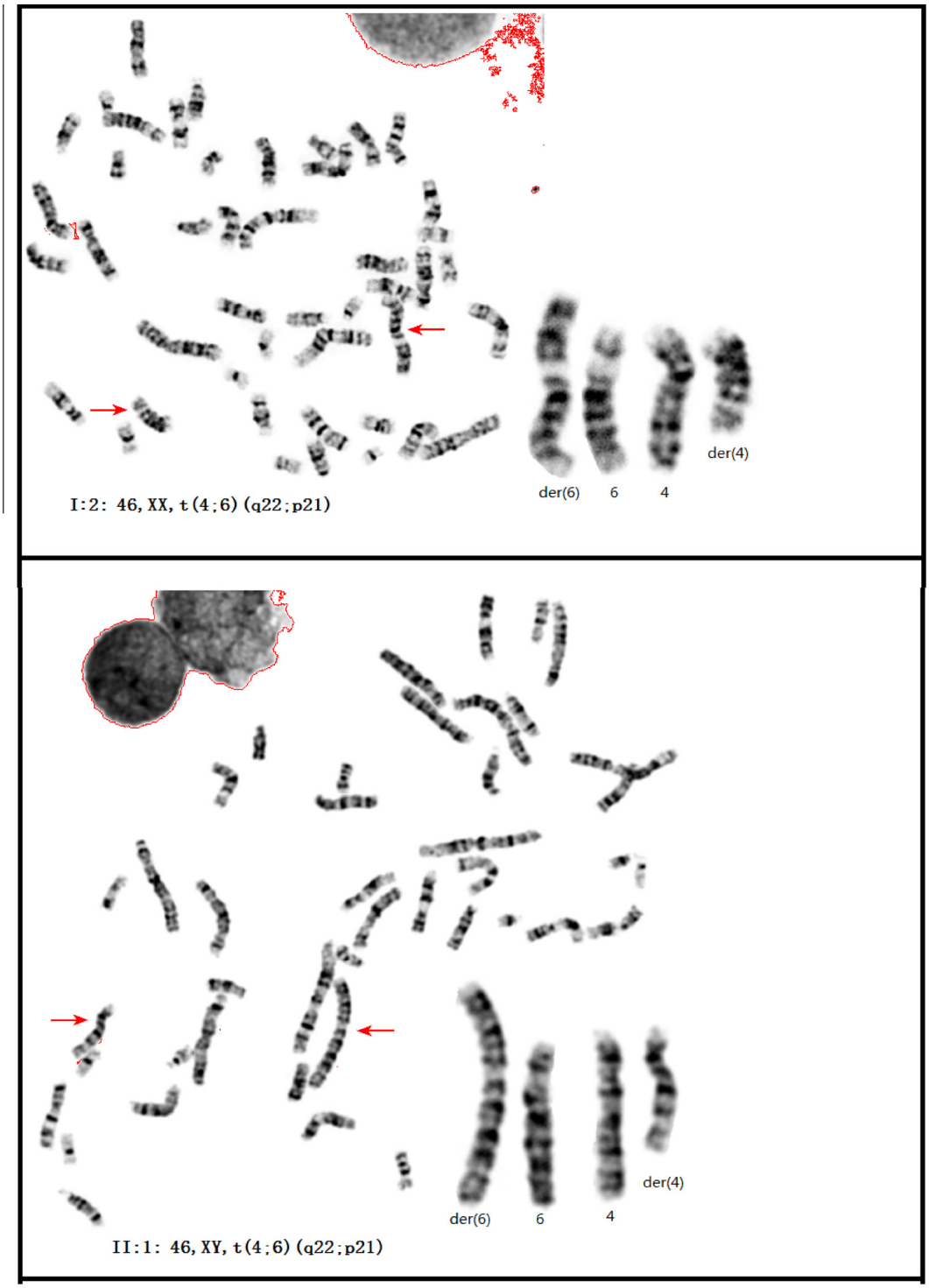
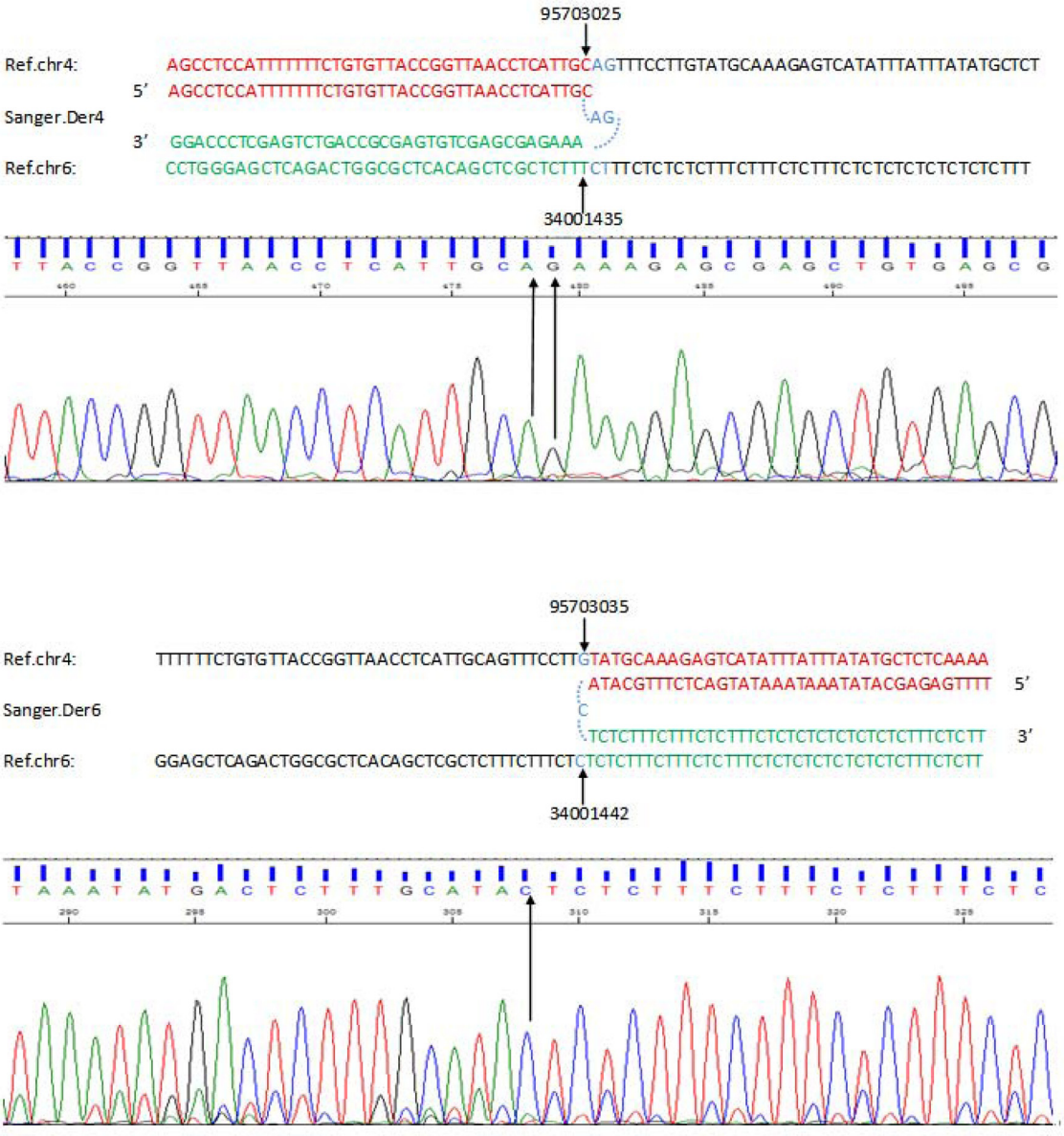
BMPR1B mutation causes Pierre Robin sequence

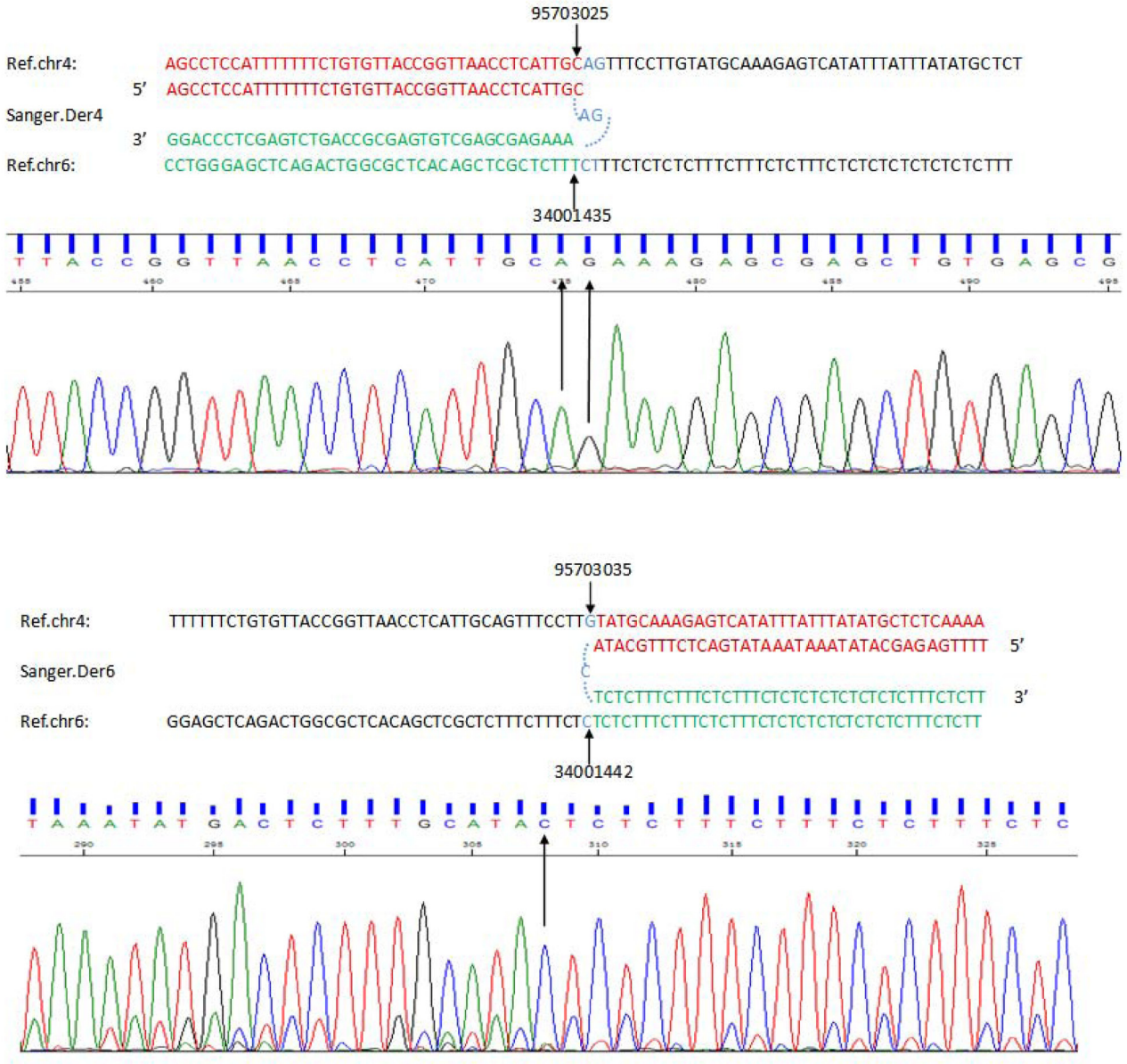
Supplementary Material



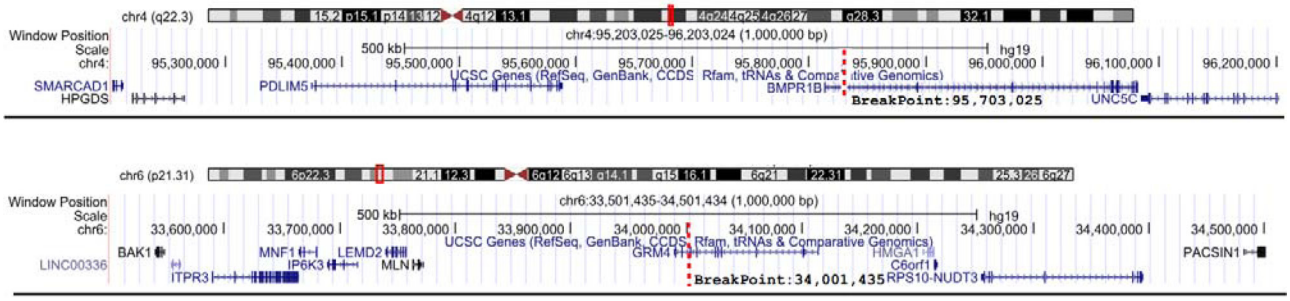
Supplementary Figure 1: The karyotypes of the family 01. GTG-banding carried on I:2 and II:1 detected the karyotype of 46, XX, t(4;6)(q22;p21) and 46, XY, t(4;6)(q22;p21), respectively.



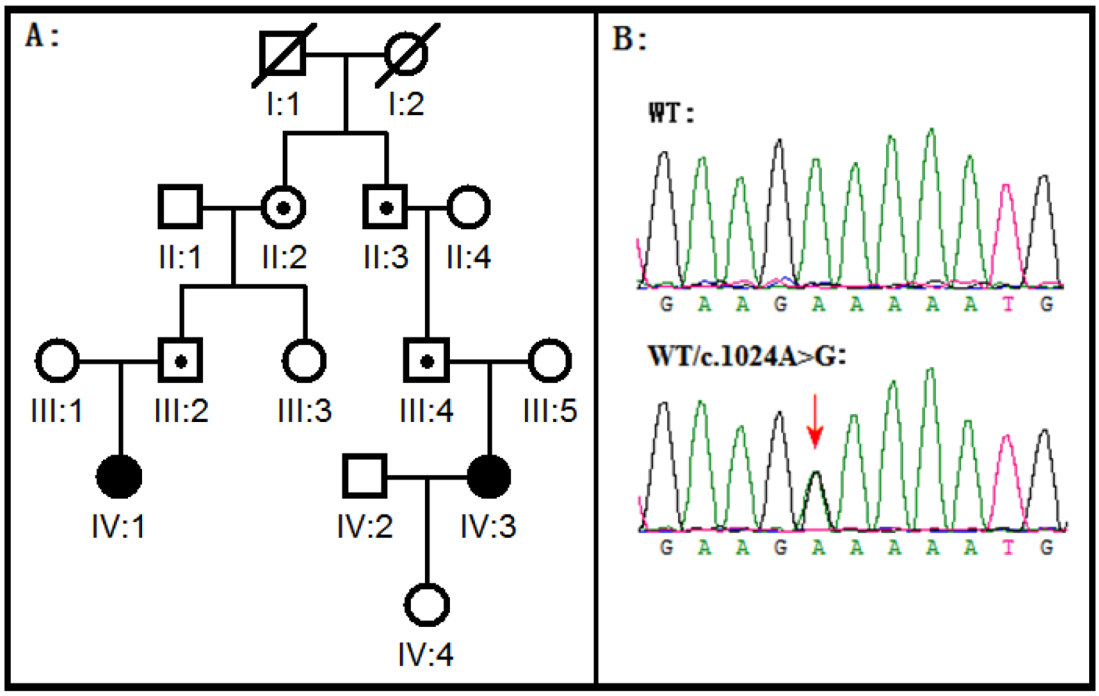
Supplementary Figure 2: On I:2 of family 01, Sanger sequencing of the fragment derived from DER 4 and DER 6 allowed defining breakpoints at base pair resolution. The 4q22.3: 95703025 fused to the 6p21.31: 34001435. The AG was sharing sequence. The 4q22.3: 95703035 fused to the 6p21.31: 34001442. The C was sharing sequence.



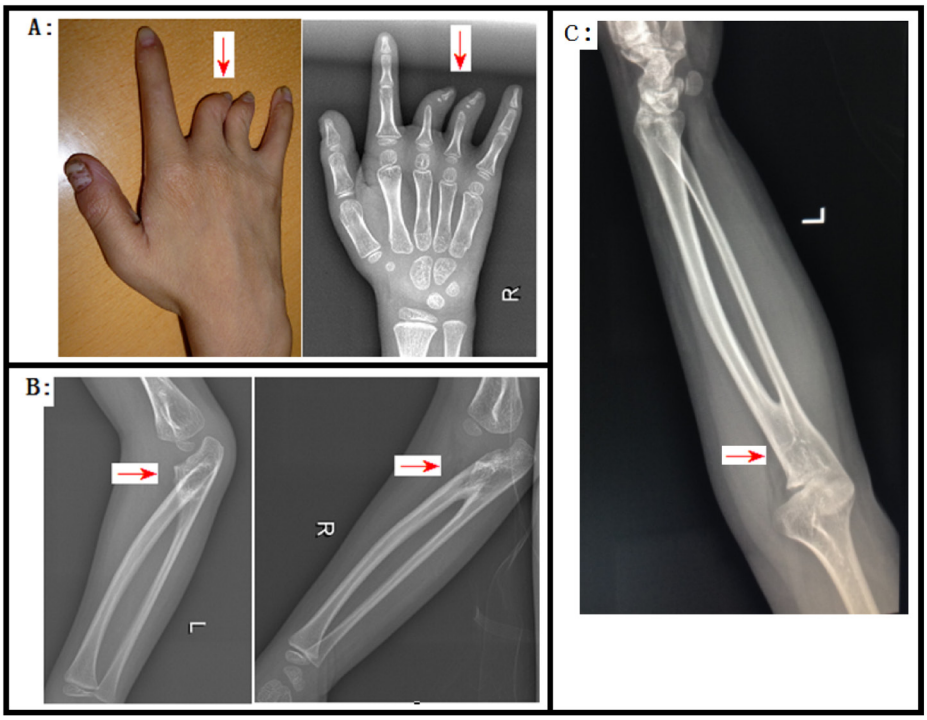
Supplementary Figure 3: On II:1 of family 01, Sanger sequencing of the fragment derived from DER 4 and DER 6 allowed defining breakpoints at base pair resolution. The 4q22.3: 95703025 fused to the 6p21.31: 34001435. The AG was sharing sequence. The 4q22.3: 95703035 fused to the 6p21.31: 34001442. The C was sharing sequence.



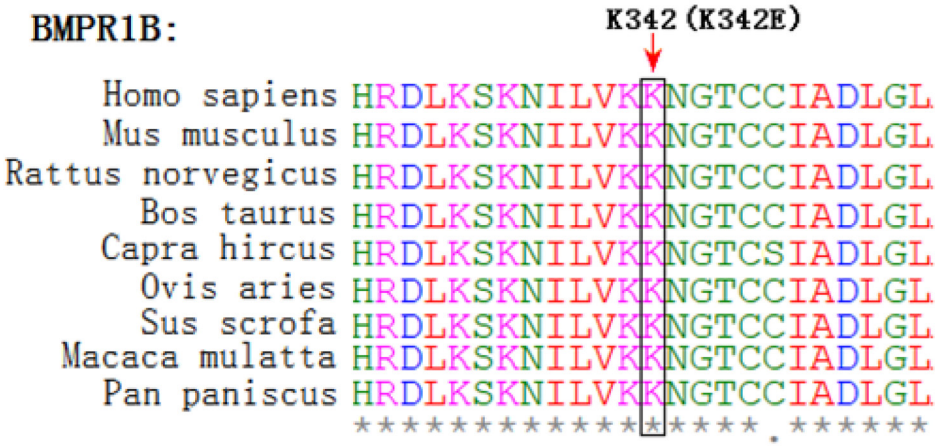
Supplementary Figure 4: The overview of the 4q22 and 6p21 breakpoints in the PRS family 01.



Supplementary Figure 5: The family 03 and the BMPR1B variant c.1024A>G. (a) The pedigree of family 03; (b) Sequence chromatograms of the BMPR1B missense variant (c.1024A>G/ p.Lys342Glu). This variant (upper) was detected on the family cases II:2, II:3, III:2, III:4, IV:1 and IV:3 but not on II:1, II:4, III:1, III:3, III:5, IV:2 and IV:4.



Supplementary Figure 6: The phenoypes of the family 03 with BMPR1B c.1024A>G. The IV:1 exhibited bilateral radioulnar synostosis (A) and the unilateral phalangeal dysplasia (b). The IV:3 exhibit unilateral radioulnar synostosis.



Supplementary Figure 7: A multiple alignment of the amino acid sequence of Homo sapiens with the orthologous proteins Mus musculus, Rattus norvegicus, Bos Taurus, Capra hircus, Ovis aries, Sus scrofa, Macaca mulatta, and Pan paniscus for protein BMPR1B.

Supplementary Table 1: Primer for cDNA amplification:

Primers for the detection of splicing effects in family 02		
Name	primer sequence	size
bmpr1b-13f	CCGCGGGTTCAGACTTCT	220bp
bmpr1b-13r	GGACAATGGTGGTGGCATTT	
bmpr1b-24f	AGGAAGATCATTTCATGCCTTGT	233bp
bmpr1b-24r	TGGTGGCATTTACAACGCAA	
bmpr1b-25f	AGGAAGATCATTTCATGCCTTGT	244bp
bmpr1b-25r	CAGAAGTGACCACAGGCAAC	
Primers for the detection of fusion-genes in family 01		
der4-1f	AGACCGCGGCGCTGAGGA	391bp
der4-2f	CGCTGAGGACGCGGGAGC	
der4-3f	CTGAGGACGCGGGAGCCG	392bp
der4-1r	TGGACTCGCTAGATTGCATGGT	
der4-2r	TGCTCAGCTCCATGGACTCG	491bp
der4-3r	TGAACTTGTTGGACATGGTGGC	
der6-1f	GACCAGCGGACACTCGAC	490bp
der6-1r	GTCATCCTCTTCTATCATCGTGA	
der6-2f	ACTCGGTGGTGGACTTCC	255bp
der6-2r	GTGAAACAATATCCGTCTGTGC	
der6-3f	GGCATCTGTGTGTGGTTTGT	330bp
der6-3r	TCCTCTTCTATCATCGTGAAACA	
der6-4f	GTGTGGTTTGTGGTGGACC	221bp
der6-4r	TGAAAATCTGAGCCTTCTAGTCC	
der6-5f	CAGGACCAGCGGACACTC	380bp
der6-5r	TCATCGTGAAACAATATCCGTCT	

Supplementary Table 2: The clinic data of seven sporadic patients with Pierre Robin Syndrome.

cases	sex	birth weight	age	karyotype	phenotype
m1666	male	2800g	12D	46, XY	pierre robbin syndrome
m1656	female	2050g	3Y	45, X[15]/46, X, r(X)[3]	pierre robbin syndrome, short stature
m1634	male	3100g	6D	46, XY	pierre robbin syndrome
m1596	male	1900g	1M	46, XY	pierre robbin syndrome
m1591	female	2200g	3D	46, XX	pierre robbin syndrome, radio ulnar synostosis and aricular anormaly
m1534	male	3250g	4D	46, XY	pierre robbin syndrome
m1529	male	2800g	1Y2M	46, XY	pierre robbin syndrome