Figures and Figure Legends

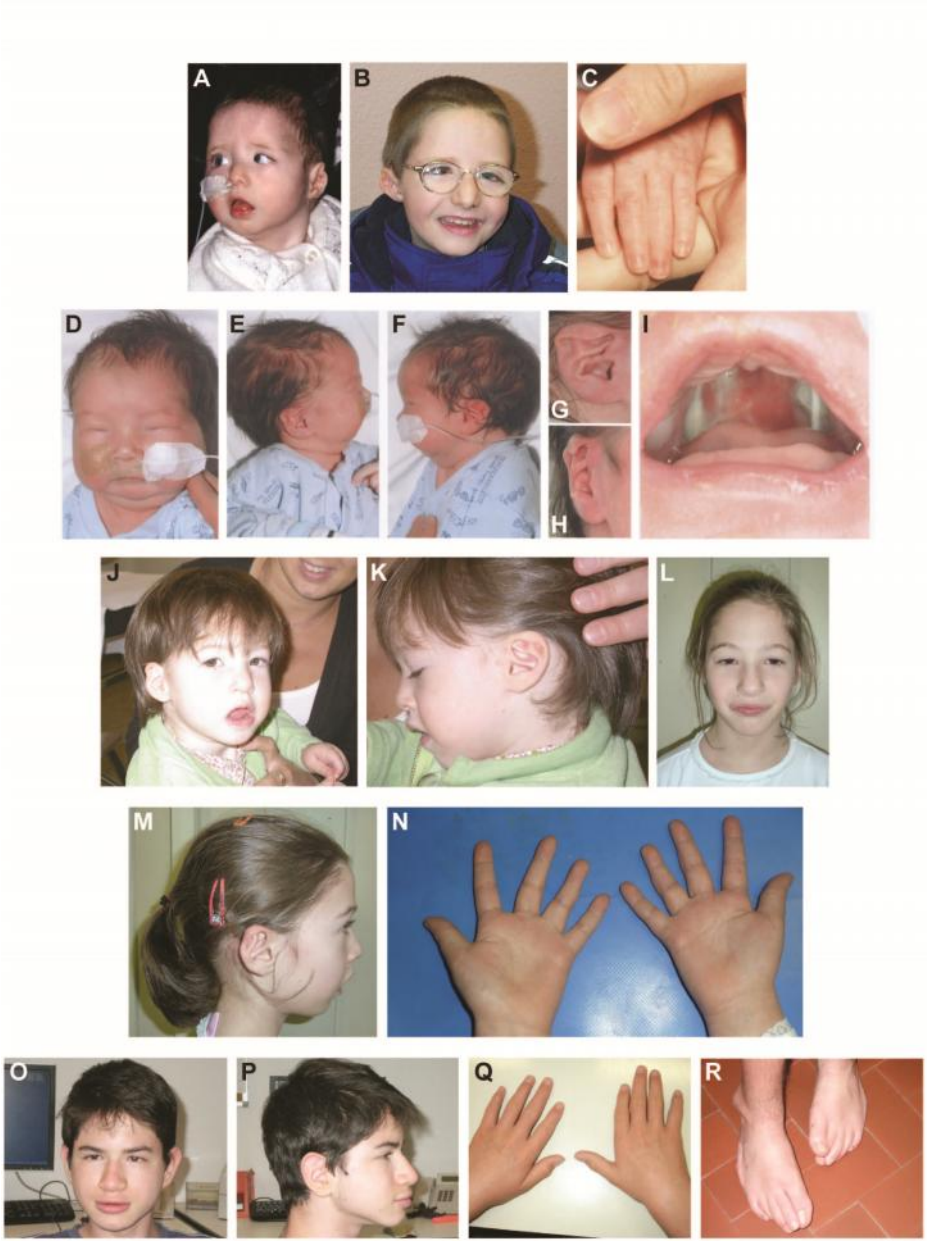

Figure 1. Photographs of cases who define the PRS critical region. **A-B:** AP facial images of Individual 1 at the ages of 1 and 7 years respectively showing down-slanting palpebral fissures, iris colobomas, prominent columella and micrognathia. **C:** Photograph of mild arachnodactyly of the upper limb in Individual 1. **D-F:** AP and lateral facial images of Individual 2 at the age of 4 weeks showing micrognathia with nasogastic feeding tube required due to prolonged feeding difficulty. **G-H:** Lateral

and oblique photograph of the right ear of Individual 2 showing overfolded and crumpled helix. **I:** Photograph showing wide cleft of the palate in Individual 2. **J-K:** AP and lateral facial photographs of Individual 3 at the age of 2 years showing mild epicanthus and external ear anomalies; helical notch on the right with prominent crus and superior crus bilaterally. **L-M:** AP and lateral facial images of Individual 3 at the age of 9 years. **N:** Photograph of palmar aspect of both hands in Individual 3 showing the absence of both contractures and arachnodactyly. **O-P:** AP and lateral facial photographs of Individual 6 showing normal ears and jaw size. **Q-R:** Photographs of hands and feet showing arachnodactyly and tapering digits.

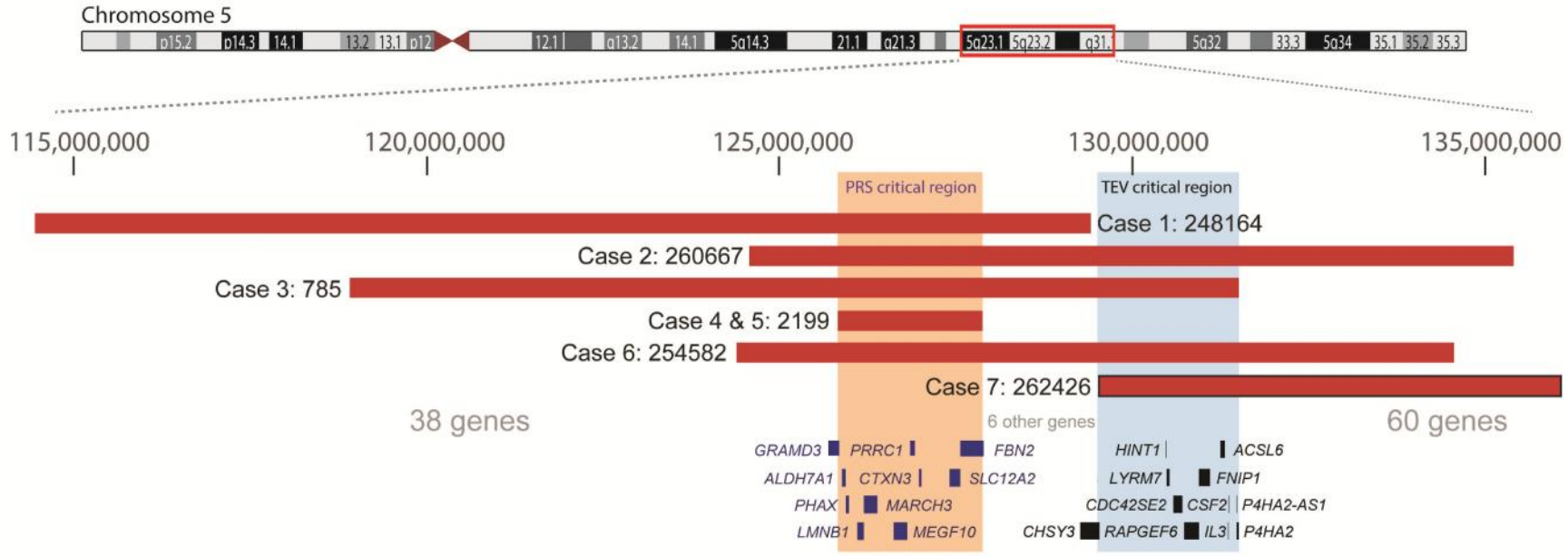

Figure 2. PRS Critical Region: Diagrammatic representation of the genomic region encompassing all of the deletions. The light orange box labelled "PRS critical region" shows the region of overlap of the 5/6 deletions that are associated with features of Pierre Robin sequence (PRS)

or cleft palate (chr5:125,794,639-127,873,679, hg19). The blue box marked “TEV critical region” shows the overlap of the four deletions of this region in which talipes equinovarus (TEV) is a feature (chr5:129,439,502-131,550,089, hg19). The figures over the tick marks at top of the image are the genomic coordinate from hg19. The red bars represent the span of the deletions from each of the families documented in the text. The red bar with black outline is the adjacent case (Individual 7) who does not show any features of PRS. The genes that are located within the critical regions are shown at the bottom of the figure.

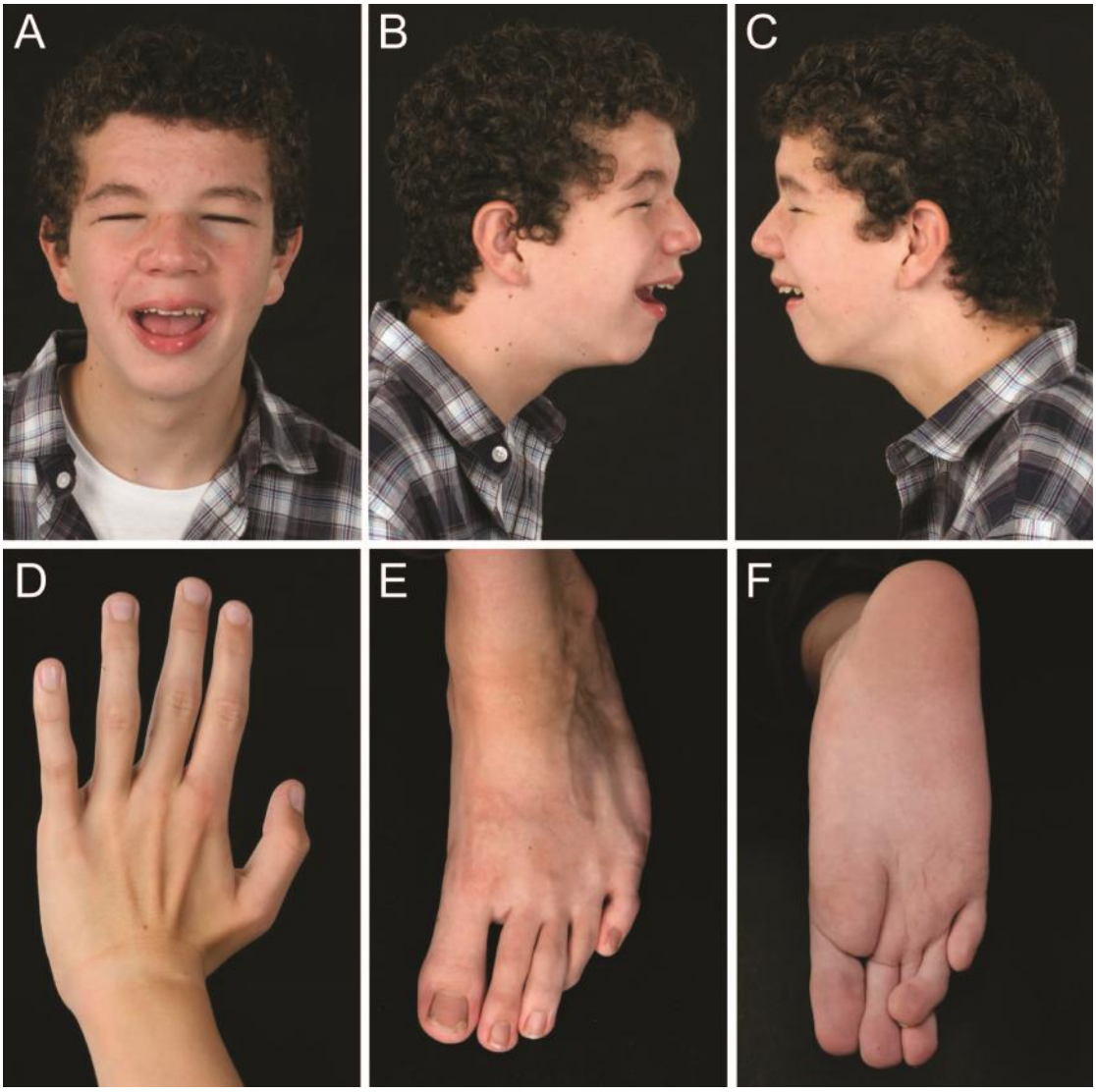

Figure 3. Photographs of the case with adjacent deletion. **A-C:** AP and lateral images of Individual 7 at the age of 14 years showing facial features somewhat reminiscent of Williams-Beuren syndrome with mild retrognathia. **D-E:** Arachnodactyly without contractures in both hands and feet in Individual 7. **F:** Platar crease and over-riding fourth toe in right foot of Individual 7.

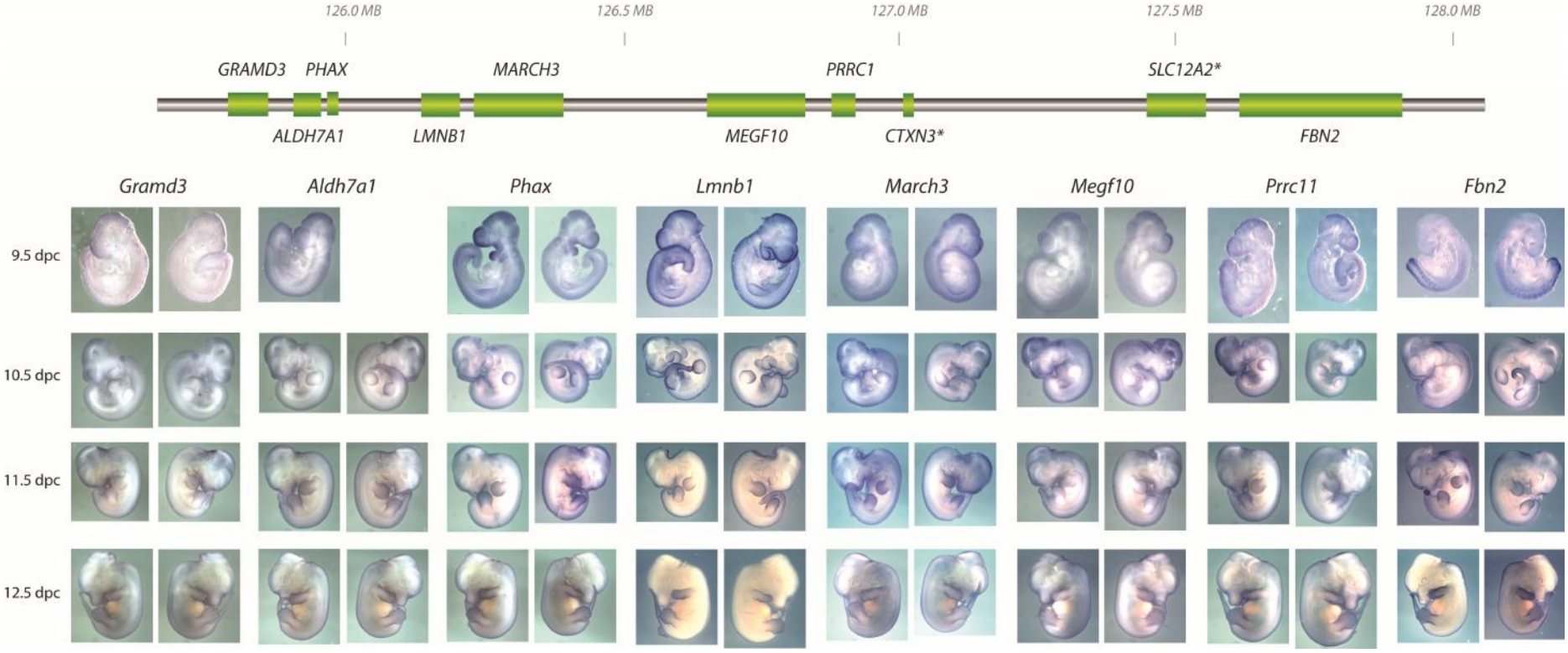

Figure 4. Expression in mouse embryos of orthologous genes mapping to the PRS critical region. The top panel shows a cartoon of the 2,079,041 bp critical region representing the genomic interval chr5:125,794,639-127,873,679 (hg19). Below this are panels showing representative right and left lateral photomicrographs of 9.5-12.5 days post coitus (dpc) mouse embryos following WISH analysis using

antisense riboprobes designed to target the 3'UTR of the genes indicated at the top of these photographs. *Gramd3, Aldh7a1, March3, Megf10* and *Prrc1* showed no evidence of site- or stage-specific expression above the BM purple stain background. *Lmnb1* showed some expression in the developing limbs. *Phax* and *Fbn2* each show clear evidence of specific developmental expression. The genes marked with an asterix (*CTXN3* and *SLC12A2*) are human genes for which a suitable mouse-specific riboprobe could not be made.

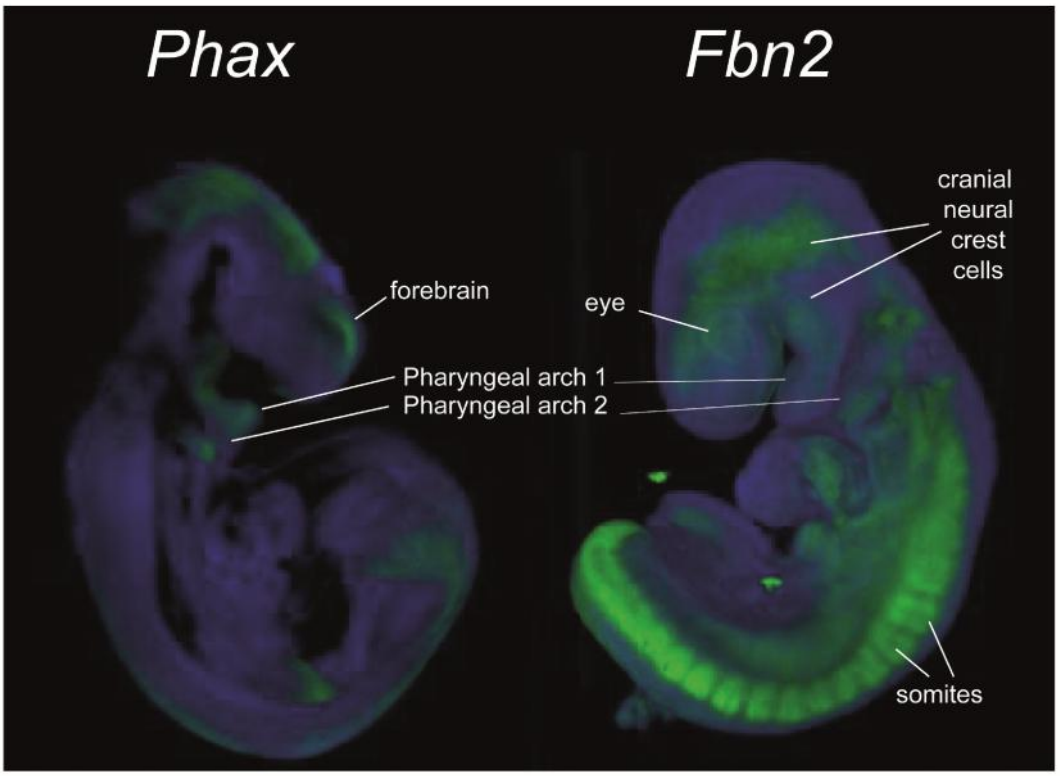

Figure 5. Optical projection tomography (OPT) images of the whole mount *in situ* hybridization using 9.5 dpc mouse embryos using antisense riboprobes for *Phax* and *Fbn2*. *Phax* (left) and *Fbn2* (right) expression is represented in green. Strong expression of Phax is seen in pharyngeal arch 1 and 2 and the forebrain. Fbn2 is most strongly expressed in the developing somites but is also seen in the developing eye, migratory neural crest cells and in pharyngeal arch 1 and 2.