Supplemental Fig. 1 Photos of patient 1 at 10 months, 2 years, and 5 years of age. Note the mild dysmorphic features including enophtalmia, long and smooth philtrum, thin upper lip vermilion, and the prominent chin with horizontal crease.

Supplemental Fig. 2. Physical map of the short arm of chromosome 16 (16p13.11p11.2)" according to UCSC Genome Browser (GRCh37/hg19) showing the genomic coordinates, the genes at the 16p13.11p11.2 region, the BAC probes, and segmental duplications. The BAC probe RP11-489O1 (red) is proximal to udSD, the BAC probe RP11-152L13 (green) is distal to BP1, and the BAC probe CTD-2515C15 (blue) is located between BP2 and BP3. OMIM-morbid genes are depicted in dark green.

Supplemental Fig. 3 Whole genome sequencing data from patient 1. A. Wisecondor log2 ratios along chromosome 16 for patient 1. Log2 ratios ranging from -0.4 to +0.4 are plotted in gray. Log2 ratios ≥ 0.4 are plotted in blue and log2 ratios ≤ 0.4 are plotted in red. The genomic gain involving the 16p13.11p11.2 locus is clearly detected, as a triplication between the genomic positions 14.890.000-28.350.000 and as a duplication between the genomic positions 28.480.001-29.050.000 (according to human genome Build GRCh37/hg19). **B.** Allelic frequencies for SNVs called by GATK Haplotypecaller (version 4) along chromosome 16. The graph shows at the triplicated locus four bands of SNPs: at BAF (B allele frequency) = 1 (BBBB), at BAF = 0.25 (genotype BAAA), at BAF=0.5 (genotype BBAA), and at BAF=0.75 (genotype BBBA). Positions with 0% of alternative allele, BAF=0 (AAAA) are not called.