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# Supplementary Methods

# Inclusion criteria

# severe isolated growth hormone deficiency(IGHD)

# Severe IGHD is defined as a peak GH level <3 ng/mL on provocative testing and combination with a diagnostic IGHD based on clinical, laboratory, and imaging information. Diagnostic criteria of IGHD in China:1. height more than 2sds below the population mean;2. decreased height velocity; 3.retarded bone age ;4.symmetrical short stature;5.normal intelligence; 6.decreased serum IGF-1 concentration;7.peak GH concentration after stimulation <10 ug/L (two independent provocation tests);8. without other pituitary hormone deficiency.

# multiple pituitary hormone deficiency(MPHD)

The anterior lobe of the pituitary gland, which produces GH, also expresses and secretes five additional hormones: PRL, TSH, FSH, LH, and ACTH. The MPHD was applied for patients with more than one pituitary hormone deficiency in addition to GHD.

# unequivocal growth hormone insensitivity(GHI)

GHI is characterised by short stature, IGF-1 deciency and normal/elevated serum GH, based on peak GH ≥ 7 μg/L or baseline GH of ≥10 ng/mL ,and IGF-1 SDS≤-2.0.（IGF-1 was expressed as SDS based on age/sex ranges provided）

# small for gestational age (SGA) without catch-up growth

# SGA has been defined either as being below the 10th percentile for weight at a given gestational age or as having a birth length or weight SD < 2.0 (below the 2.3 percentile). SGA was not catch up to stature above -2sd within the age of 2 years was defined as without catch-up growth.

# additional congenital anomalies or dysmorphic features

# "Congenital abnormalities" or "deformed features" are defined as congenital defects, commonly including congenital heart disease, cleft lip and palate, limb defects, special facial features, etc. Dysmorphic features refers to The Human Phenotype Ontology (HPO), HPO provides a standardized vocabulary of phenotypic abnormalities encountered in human disease. https://hpo.jax.org/app/

# evidence of a skeletal dysplasia

Definition of a skeletal dysplasia is a generalised structural abnormality of bone and cartilage growth and modelling. There are many ways in which a skeletal dysplasia may present, include short long bones or abnormal mineralization on prenatal ultrasound, disproportionate short stature, fractures, or metaphyseal changes, etc.

# associated intellectual disability(ID) or developmental delay(DD)

# Patients with developmental/intelligence quotient (DQ/IQ)＜70 were characterized as developmental delay(DD) or intellectual disability(ID).

# microcephaly

# Microcephaly is defined as a head circumference more than two standard deviations below the mean for gender and age.

# mother with recurrent miscarriage

# Recurrent miscarriage is classically defined as the loss of three or more consecutive pregnancies before the 20th week of gestation.

# height below -3SDS

# Height below -3SDS compared with the population mean or mid-parental target height

# Exclusion criteria

# such as Down’s syndrome, Turner syndrome with typical phenotypes (confirmed by karyotyping)

# Turner syndrome with typical phenotypes or Down’s syndrome had been directly confirmed by karyotyping. However, some patients with atypical phenotypes could not be diagnosed by clinical features and these patients will be enrolled in the study.

# pituitary tumor

**short stature secondary to chronic illness**

# Short stature or growth failure may be caused by chronic illness, such as chronic kidney disease, celiac disease, inflammatory bowel disease, tumors, etc. All patients received systematically assessment to exclude chronic illness including medical history inquiry, physical examinations, and necessary laboratory tests.

# with definitive genetic diagnosis

# Supplementary Table 1. 70.4% (131/186) patients with facial dysmorphism were identified with P/LP variants, related to 52 genes.

|  |  |  |  |
| --- | --- | --- | --- |
| P/LP variants | No. of cases | | Identified variants (no. of patients affected) |
| Variants in genes | | 98 | *PTPN11*(17)*,FGFR3(10),NIPBL(6),IDS(5),KMT2A(4),COL2A1(3),FGFR2(3),SOS1(3),RAF1(2),KMT2D(2),OBSL1(2),CREBBP(2),GNPTAB*(2),*GH1(1),ACAN(1),COL1A1(1),COL3A1(1)BLM*(1)*,ERCC6*(1)*,CUL7*(1)*,CHD7*(1),*HDAC8*(1)*,SMC1A*(1),*SMC3*(1),*LMNA*(1),*ORC6*(1),*PCNT*(1),*KDM6A*(1),*ANKRD11*(1),*FGD1*(1)*FAM111A*(1)*MAP2K1*(1),*HRAS*(1),*KAT6B*(1),*BRAF*(1),*KRAS*(1),*RIT1*(1),*SHOC2*(1),*NBAS*(1),*TWIST1*(1),*EFNB1*(1),*TFAP2A*(1),*GJA1*(1),*PAX3*(1),*THRA*(1),*TPO*(1),*ARSB*(1) ,*GUSB*(1), *LMX1B*(1),*NOTCH2*(1),*OFD1*(1)*,POGZ*(1),*POC1A*(1) |
| Chromosomal abnormalities and CNVs | 33 | | Turner syndrome (3)  22q11.2 deletion syndrome (3)  Williams-Beuren syndrome (3)  Chromosome 18p deletion syndrome (3)  17p13.3 deletion syndrome (3)  del(4)(p16.3)[hg19,(chr1:168,250,278-173,886,516)](over 5000kb);dup(21)(q22.3)[hg19,(chr21:46,305,869-47,865,682)](over 1500kb)(1)  del(1)(p36.33-p36.23 )[hg19,(chr1:955,503-7,829,766)](over 6800kb) (1)  dup(1)(q42.13-q44)[hg19,(chr1:229,566,993-247,612,406)](over 18000kb);del(15)(q26.3)[hg19,(chr15:99,191,768-101,792,253)](over 1600kb) (1)  del(2)(q32.3-q33.2)[hg19(chr2: 193,730,505-204,701,813)](10971kb) (1)  del(2)(q24.2-q31.1)[hg19(chr2: (157205510-170457666)](13252kb) (1)  del(2)(q37.3[hg19,(chr2:239,152,679-242,708,231)](over 3500kb) (1)  del(2)(q37.3)[hg19,(chr2:239,969,864-242,708,231)](over 2700kb);dup(9)(q34.3)[hg19,(chr9:140,149,752-140,730,578)](over 500kb) (1)  dup(6)(p25.3-p22.3)[hg19,(chr6:391,739-18,155,400)](over 17000kb) (1)  del(6)(p21.1)[hg19,(chr6:41,126,244-43,021,683)](over 1900kb) (1)  del(7)(q33-q35)[hg19,(chr7:137,761,205-144,533,146)](over 6700kb) (1)  del(7)(q36.1-q36.3)[hg19,(chr7:150,642,044-157,210,133)](over 6500kb);dup(18)(q23)[hg19,(chr18:77,439,801- 77,514,510)](over 200kb)(1)  del(8)(q23.3-q24.11)[hg19,(chr8:116,420,724-119,124,058)](over 2700kb)(1)  del(9)(q31.2-q31.3)[hg19,(chr9:108,320,411-113,563,278)](over 5200kb) (1)  del(9)(q21.11-q21.31)[hg19,(chr9:71000154-83236029)](12236kb) (1)  del(16)(p13.11)[hg19,(chr16:15,737,124-16,317,328)(over 500kb) (1)  dup(17)(p11.2)(over 3000kb) (1)  del(22)(q13.2)[hg19,(chr22:41,488,614-41,924,993)](over 400kb) (1)  dup(X)(q26.3-q28) [hg19,(chrX:135,067,586-149,841,616)] (over 14800kb) (1) |

# Supplementary Table 2. 53.1%(51/96) patients with DSD were identified with P/LP variants in our cohort.

|  |  |  |
| --- | --- | --- |
| P/LP variants | No. of cases | Identified variants (no. of patients affected) |
| Variants in genes | 34 | *PTPN11*(8),*GLI2*(3),*FGFR1*(2),*GH1*(1),*GHR*(1),*SOX3*(1),*ERCC6*(1),*CHD7*(1),  *NIPBL*(1),*ORC6*(1),*CREBBP*(1),*SOX11*(1),*KMT2A*(1),*GNAS*(1)  ,*MAP2K1*(1),*RAF1*(1),*SOS1*(1),*BBS2*(1),*SOX2*(1),*PEX26*(1),  *DUOX2*(1),*PAX8*(1), *AR*(1), *KMT2C*(1), *SLC12A3*(1) |
| Chromosomal abnormalities and CNVs | 17 | Turner syndrome (4)  45X/46XY mosaicisms (2)  47XXY (1)  del(18)(p11.31-p11.21)[hg19,(chr18:2,916,992-12,884,236)] (over10000kb) (1)  del(17)(p13.3)[hg19,(chr17:1,247,834-1,680,868)] (over 400kb)(1)  del(17)(p11.2)[hg19,(chr17:17,115,527-19,580,909)] (over 2400kb)(1)  del(17)(p12-p11.2)[hg19(chr17:15,801,183-20,274,157)](4473kb)(1)  del(1)(q24.3-q25.3)[hg19(chr1:171,130,803-185,746,128)(14615kb)(1)  del(5)(p15.33-p15.1)[hg19,(chr5:218,338-16,617,094)](over 16000kb)(1)  del(7)(q33-q35)[hg19,(chr7:137,761,205-144,533,146)](over 6700kb)(1)  del(22)(q13.2)[hg19,(chr22:41,488,614-41,924,993)](over 400kb)(1)  del(22)(q12.3-q13.1)[hg19,(chr22:36,649,117-38,380,539)](over 1700kb)(1)  dup(22)(q11.23)[(hg19)chr22:23,648,768-24,995,964](1347kb)(1) |

# Supplementary Table 3. 39 male patients (46 XY) were diagnosed with cryptorchidism, 66.7% (26/39) patients were identified with P/LP variants.

|  |  |  |
| --- | --- | --- |
| P/LP variants | No. of cases | Identified variants (no. of patients affected) |
| Variants in genes | 19 | *PTPN11*(8)*,MAP2K1*(1)*,RAF1*(1),*SOS1*(1),*GH1*(1),*GLI2*(1),  *NIPBL*(1), *CREBBP*(1),*SOX11*(1),*KMT2A*(1),*BBS2*(1),  *PEX26*(1) |
| Chromosomal abnormalities and CNVs | 7 | 47XXY (1)  del(18)(p11.31-p11.21)[hg19,(chr18:2,916,992-12,884,236)] (over10000kb)(1)  del(17)(p13.3) [hg19,(chr17:1,247,834-1,680,868)] (over 400kb)(1)  del(17)(p12-p11.2)[hg19(chr17:15,801,183-20,274,157)](4473kb)(1)  del(1)(q24.3-q25.3)[hg19(chr1:171,130,803-185,746,128)(14615kb)(1)  del(5)(p15.33-p15.1)[hg19,(chr5:218,338-16,617,094)](over 16000kb)(1)  dup(22)(q11.23)[(hg19)chr22: 23,648,768-24,995,964](1347kb)(1) |

# Supplementary Table 4. 53.3% (49/92) patients with CHD were identified with P/LP variants, related to 14 genes, 9 CNVs and 1 chromosomal abnormalities.

|  |  |  |
| --- | --- | --- |
| P/LP  Variants | No. of cases | Identified variants (no. of patients affected) |
| Variants in  Genes | 31 | *PTPN11*(13)*,RAF1*(2)*,SHOC2(2),SOS1(2),ANKRD11(2)IDS(2),,FBN1(1),*  *NIPBL(1),KMT2A(1),NF1(1),KRAS(1),RIT1(1),PEX26(1),GNPTAB(1)* |
| chromosomal abnormalities and CNV | 18 | 22q11.2 deletion syndrome (5)  Williams-Beuren syndrome (4)  Turner syndrome (2)  del(18)(p11.31-p11.21)[hg19,(chr18:2,916,992-12,884,236)](over 9900kb) (1)  del(17)(p13.3)[hg19,(chr17:1,247,834-1,680,868)](over 400kb) (1)  del(2)(q32.3-q33.2)[hg19(chr2:193,730,505-204,701,813)](10971kb) (1)  del(2)(q24.2-q31.1)[hg19(chr2:(157205510-170457666)](13252kb) (1)  dup(2)(p25.3)[hg19,(chr2:1,417,233-3,750,260)](over 2300kb) and del (11) (q24.1-q25) [hg19,(chr11:122,942,714-134,135,746)](over 1200kb)(1)  del(9)(q21.11-q21.31)[hg19,(chr9:71000154-83236029)](12236kb) (1)  del(13)(q31.1-q32.1)[hg19,(79,314,118-96,544,277)](17230kb) (1) |

# Supplementary Table 5. 64.7% (152/235) patients with skeletal dysplasia were identified with P/LP variants. Pathogenic variants were identified in 59 genes and 6 CNVs.

|  |  |  |
| --- | --- | --- |
| P/LP variants | No. of cases | Identified variants (no. of patients affected) |
| Variants in genes | 146 | *FGFR3*(29),*PHEX*(11),*PTPN11*(11),*IDS(9),COL2A1*(5),*SHOX*(4),*GNAS*(4),*RUNX2* (4), *EXT1* (4), *NF1*(2), *COMP* (3),*ACAN* (3), *COL1A1*(3),*FGFR2* (2), *FAM111A* (1),*CLCN7*(2), *ARSB* (2), *GNPTAB* (2),*TRPS1*(2)*TRPV4*(2),*OFD1*(2), *NPR2*(2),*WISP3*(1), *GLI2*(1),*COL1A2*(1),*COL3A1*(1),*COL10A1*(1), *COL11A1*(1),*FBN1*(1),*PTHLH*(1),*ERCC6*(1),*CUL7*(1),*OBSL1*(1),*HDAC8*(1),*LMNA*(1),*ANKRD11*(1),*HRAS*(1),*KRAS*(1),*RAF1*(1),*RIT1*(1),*SHOC2*(1),*SOS1*(1),*NBAS*(1),*SBDS*(1),*GALNS*(1),*TWIST1*(1),*EFNB1*(1),*GALNS*(1),*TCIRG1*(1),*TPO*(1), *GUSB*(1), *SGSH*(1),*CYP27B1*(1),*FLNA*(1), *FLNB(1)*, *LMX1B*(1), *NOTCH2*(1), *TRAPPC2*(1), *AMER1*(1)*MFN2*(1) |
| CNVs | 6 | 22q11.2 deletion syndrome (1)  dup(1)(q42.13-q44)[hg19,(chr1:229,566,993-247,612,406)](over 18000kb);del(15)(q26.3)[hg19,(chr15:99,191,768-101,792,253)](over 1600kb) (1)  del(2)(q37.3[hg19,(chr2:239,152,679-242,708,231)](over 3500kb) (1)  dup(2)(p11.2-p13.2)[hg19,(chr2:71,693,832-86,565,206)] (over 15000kb) (1)  del(8)(q23.3-q24.11)[hg19,(chr8:116,420,724-119,124,058)](over 2700kb) (1)  dup(X)(q26.3-q28) [hg19,(chrX:135,067,586-149,841,616)] (over 14800kb) (1) |

# Supplementary Table 6. 70.0% (98/140) patients with intellectual disability or developmental delay were identified with P/LP variants, related to 34 genes.

|  |  |  |
| --- | --- | --- |
| P/LP variants | Disorder/Phenotype | Identified variants (no. of patients affected) |
| Variants in genes | Wiedemann-Steiner Syndrome | *KMT2A*(5) |
| Cornelia de Lange syndrome | *NIPBL*(4) ,*HDAC8*(1), *SMC1A*(1), *SMC3*(1) |
| Kabuki syndrome | *KDM6A*(2), *KMT2D*(1) |
| KBG syndrome | *ANKRD11*(2) |
| Rubinstein–Taybi syndrome | *CREBBP*(2) |
| Cardio-facio-cutaneous syndrome | *MAP2K1*(2), *BRAF*(1) |
| Noonan syndrome | *PTPN11*(1), *RAF1*(2) |
| Costello syndrome | *HRAS* (1) |
| Say-Barber-Biesecker-Young-Simpson syndrome | *KAT6B*(2) |
| FG syndrome | *MED12*(2) |
| White-Sutton syndrome | *POGZ*(2) |
| Rett syndrome | *MECP2*(2) |
| Mucopolysaccharidosis | *IDS(1), SGSH*(1) |
| Hereditary distal renal tubular acidosis | *ATP6V1B1*(1) |
| Joubert Syndrome | *OFD1*(1) |
| Gitelman syndrome | *SLC12A3*(1) |
| Metaphyseal chondro-dysplasia, Schmid type | *COL10A1*(1) |
| Achondroplasia | *FGFR3*(1) |
| Cockayne syndrome | *ERCC6*(1) |
| MOPD II | *PCNT*(1) |
| Kenny-Caffey syndrome | *FAM111A*(1) |
| Bardet-Biedl syndrome | *BBS2*(1) |
| Saethre-Chotzen syndrome | *TWIST1*(1) |
| Claes-Jensen syndrome | *KDM5C*(1) |
| Osteopetrosis | *CLCN7*(1) |
| GRIN1-Related Neurodevelopmental Disorder | *GRIN1*(1) |
|  | MFN2 Hereditary Motor and Sensory Neuropathy | *MFN2*(1) |

# Supplementary Table 7. 70% (98/140) patients with intellectual disability or developmental delay were identified with P/LP variants.49%(48/98) patients were identified with CNVs.

|  |  |  |
| --- | --- | --- |
| P/LP  variants | No. of cases | Identified variants (no. of patients affected) |
| CNV | 48 | Williams–Beuren syndrome (4)  22q11.2 deletion syndrome (3)  1q24q25 deletion syndrome (3)  Chromosome 18p deletion syndrome (2)  Smith–Magenis syndrome (2)  1p36 deletion syndrome (2)  dup(1)(q42.13-q44)[hg19,(chr1:229,566,993-247,612,406)](over 18000kb);del(15)(q26.3)[hg19,(chr15:99,191,768-101,792,253)](over 1600kb)(1)  dup(1)(q42.2-q44)[hg19,(chr1:230,838,270-247,612,406)](over 16000kb）(1)  del(2)(q24.2-q31.1)[hg19(chr2: (157205510-170457666)](13252kb) (1)  del(2)(q37.3)[hg19,(chr2:239,152,679-242,708,231)](over 3500kb) (1)  del(2)(q37.3)[hg19,(chr2:239,969,864-242,708,231)](over 2700kb);dup(9)(q34.3)[hg19,(chr9:140,149,752-140,730,578)](over 500kb) (1)  del(2)(p21-p16.3) [hg19,(chr2:47,596,287-49,381,666)](over 1800kb) (1)  dup(2)(p24.1-16.3)[hg19,(chr2:20,110,029-51,259,674)](over 31000kb) (1)  del(4)(p16.3)[hg19,(chr1:168,250,278-173,886,516)](over 5000kb);dup(21)(q22.3)[hg19,(chr21:46,305,869-47,865,682)](over 1500kb)(1)  del(5)(p15.33)[hg19,(chr5:218,338-1,816,167)](over 1600kb)(1)  del(5)(p15.33-p15.1)[hg19,(chr5:218,338-16,617,094)](over 16000kb)(1)  dup(6)(p25.3-p22.3)[hg19,(chr6:391,739-18,155,400)](over 17000kb) (1)  del(6)(q22.1)[hg19,(chr6:116,440,085-117,923,705)](over 1400kb)(1)  del(7)(q33-q35)[hg19,(chr7:137,761,205-144,533,146)](over 6700kb) (1)  del(7)(q33-q34)[hg19,(chr7:137,761,178-140,624,728)](over 2900kb) (1)  del(7)(q36.1-q36.3)[hg19,(chr7:150,642,044-157,210,133)](over 6500kb);dup(18)(q23)[hg19,(chr18:77,439,801- 77,514,510)](over 200kb) (1)  del(9)(q33.3-q34.11)[hg19,(chr9:129,376,722-131,395,944)](over 2000kb) (1)  del(9)(q31.2-q31.3)[hg19,(chr9:108,320,411-113,563,278)](over 5200kb) (1)  del(9)(q21.11-q21.31)[hg19,(chr9:71000154-83236029)](12236kb)(1)  del(10)(q26.13-26.2)[hg19,(chr10:124,221,041-127,511,837)] (over 3200kb) (1)  del(12)(q24.31)[hg19,(chr12:122,755,981-124,246,301)](over 1400kb)(1)  del(12)(p13.33-p13.31) [hg19,(chr12:389,223-6,484,729)](over 6000kb) (1)  del(13)(q31.1-q32.1)[hg19,(chr13:79,314,118-96,544,277)](17230kb) (1)  del(13)(q34)(over 3000kb) (1)  del(15)(q11.2-q13.1)[hg19(23,707,494-28,525,454)](4818kb) (1)  dup(16)(p13.11)[hg19,(chr16:15,737,124-16,317,328)](over 500kb) (1)  del(16)(p13.11)[hg19,(chr16:15,737,124-16,317,328)(over 500kb) (1)  dup(17)(p11.2)(over 3000kb) (1)  dup(19)(p13.3)[hg19,(chr19:852,303-6,720,661)](over 5800kb) (1)  del(20)(p13)[hg19,(chr20:939,096-2,413,399)](over 1400kb)(1)  dup(22)(q11.23)[hg19(chr22: 23,648,768-24,995,964)](1347kb) (1)  dup(22)(q11.23)[hg19,(chr22:23,915,313-24,924,358)](over 1000kb) (1)  duplication of *ARID1B* gene (1) |

**Supplementary Table 8. 56.3%(9/16) patients with microcephaly were identified with P/LP variants, related to 6 genes and 4 CNVs.**

|  |  |  |
| --- | --- | --- |
| P/LP variants | Disorder/  Phenotype | Identified variants (no. of patients affected) |
| Variants in genes | Bloom syndrome | *BLM*(1) |
| Cockayne syndrome | *ERCC6*(1) |
| Cornelia de Lange syndrome | *NIPBL*(1), *SMC1A*(1) |
| MOPD II | *PCNT*(1) |
| Hereditary distal renal tubular acidosis | *ATP6V1B1*(1) |
| Microcephaly, facial dysmorphism,  development delay | del(2)(q24.2-q31.1)[hg19(chr2: (157205510-170457666)](13252kb)(1) |
| Microcephaly, facial dysmorphism,  development delay | del(2)(q37.3)[hg19,(chr2:239,969,864-242,708,231)](over  2700kb);dup(9)(q34.3)[hg19,(chr9:140,149,752-140,730,578)](over 500kb)(1) |
| Microcephaly,  development delay | del(10)(q26.13-26.2)[hg19,(chr10:124,221,041-127,511,837)] (over 3200kb)(1) |

**Supplementary Table 9. 143 of these patients presented with no other risk factors except for short stature (< −3 SDS), whereas 11.19% (16/143) of these patients harbored P/LP variants.**

|  |  |  |
| --- | --- | --- |
| P/LP variants | No. of cases | Identified variants (no. of patients affected) |
| Variants in genes | 12 | *KMT2A* (3), *FGFR3*(Hypochondroplasia) (2)*, IHH* (1)*, GNAS* (1)*, ACAN* (2)*, GHRHR* (1), *IGF1R* (1), *GHSR* (1) |
| Chromosomal abnormalities and CNVs | 4 | del(6)(q25.1-q25.2)[hg19,(chr6:149,539,060152,958,497)  ](over 3400kb) (1)  dup(16)(p11.2)(over 300kb) (1)  large deletion of Xp and large duplication of Xq(1)  del(X)(p22.33-p22.32)[(hg19(chrX: 60,701- 4,664,247)] (over 4600kb)(include *SHOX* gene) (1) |

# 

# Supplementary Table 10. Detailed phenotypes and genetic results of 361 patients were identified with P/LP variants.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient ID | Gender | Age | Phenotype | Genetic results |  |  |  | Inheritance | ACMG category |
| 6135 | male | 15y | severe IGHD | *GH1* | NM\_000515.4:c.242\_243del | p.(Ser81\*) | Homozygote | F/M | P |
| 6515 | male | 4y | severe IGHD,cryptorchidism,small pituitary size | *GH1* | NM\_000515.4:c.291+1G>A | p.? | Heterozygote | De novo | P |
| 10010 | male | 2y11m | severe IGHD,big and protruding foreheads,small pituitary size | *GH1* | NM\_000515.4:[c.240del]/[Exon 1-5 del] | [p.(Ser81Glnfs\*19)]/[p.?] | Compound heterozygote | F/M | P |
| 6500 | male | 5y | SGA,female external genitalia, suspicious uterine-like structure between bladder and rectum, absent ovaries or testes, | *GHR* | NM\_000163.4: c.136+1G>A | p.? | Homozygote | F/M | P |
| 5410 | male | 5y | short stature | *GHRHR* | NM\_000823.3:c.1147G>T | p.(Val383Leu) | Homozygote | F/M | LP |
| 5175 | male | 12m | MPHD,micropenis, small testes, anterior pituitary hypoplasia, | *GLI2* | NM\_005270.4:c.3463\_3464del | p.(Asp1155Argfs\*39) | Heterozygote | De novo | P |
| 5589 | male | 2y3m | MPHD,micropenis,  small testes, anterior pituitary hypoplasia, | *GLI2* | NM\_005270.4:c.3137del | p.(Gly1046Alafs\*84) | Heterozygote | M | LP |
| 6606 | male | 4y | MPHD,micropenis,  small testes,  deafness, intellectual disability,anterior pituitary hypoplasia | *GLI2* | NM\_005270.4: c.3640C>T | p.(Gln1214\*) | Heterozygote | M | LP |
| 6845 | male | 3y | short stature | *GHSR* | NM\_198407.2:c.107\_109del | p.(Gln36del) | Heterozygote | F | LP |
| 9601 | male | 9y | short stature | *IGF1R* | NM\_000875.4:c.179A>C | p.(His60Pro) | Heterozygote | De novo | LP |
| 13921 | female | 5y9m | short stature,SGA | *IGF1R* | deletion (whole gene) |  |  |  | P |
| 3973 | male | 11y | severe IGHD,small penis,mild learning difficulties,anterior pituitary hypoplasia | *SOX3* | NM\_005634.2: c.424C>A | p.(Pro142Thr) | Heterozygote | M | LP |
| 2321 | male | 12y | short stature | *ACAN* | NM\_013227.3:c.661del | p.(Tyr221Metfs\*10) | Heterozygote | M | P |
| 4212 | male | 5y | short stature | *ACAN* | NM\_013227.3:c.436delC | p.(Leu146Trpfs\*5) | Heterozygote | M | P |
| 14569 | male | 10y11m | knee valgus deformity | *ACAN* | NM\_013227.3:c.1180C>T | p.(Arg394\*) | Heterozygote | F | P |
| 11292 | female | 2y | skeletal dysplasia | *ACAN* | NM\_013227.3: c.4486del | p.(Val1496\*) | Heterozygote | F | P |
| 11550 | female | 7y | skeletal dysplasia,facial dysmorphism | *ACAN* | NM\_013227.3:c.1429+1del | p.? | Heterozygote | M | P |
| 11565 | female | 7y | short stature | *ACAN* | NM\_013227.3:c.11T>G | p.(Leu4\*) | Heterozygote | F | P |
| 6533 | female | 6y | short stature,SGA | *COL1A1* | NM\_000088.3:c.1171G>A | p.(Asp391Asn) | Heterozygote | De novo | LP |
| 10661 | female | 6m | skeletal dysplasia,facial dysmorphism | *COL1A1* | NM\_000088.3 c.1588G>A | p.(Gly530Ser) | Heterozygote | De novo | P |
| 14156 | male | 3y | skeletal dysplasia,frequent fracture | *COL1A1* | NM\_000088.3:c.3421C>T | p.(Arg1141\* ) | Heterozygote | De novo | P |
| 11006 | male | 15m | skeletal dysplasia,frequent fracture | *COL1A1* | NM\_000088.3:c.63\_64ins19 | p.(Gly22Glnfs\*6 ) | Heterozygote | F | P |
| 6954 | female | 2y | skeletal dysplasia,frequent fracture | *COL1A2* | NM\_000089.3: [c.749G>T]/[c.838G>A] | [p.(Gly250Val)]/[p.(Gly280Ser)] | Heterozygote | De novo | LP |
| 3832 | male | 4y | skeletal dysplasia,facial dysmorphism | *COL2A1* | NM\_001844.4:c.1826G>T | p.(Gly609Val) | Heterozygote |  | LP |
| 4042 | male | 4y | short stature,SGA | *COL2A1* | NM\_001844.4:c.1016G>A | p.(Gly339Asp) | Heterozygote | De novo | LP |
| 6967 | male | 2y | skeletal dysplasia,facial dysmorphism | *COL2A1* | NM\_001844.4:c.1942-2A>G | p.? | Heterozygote | De novo | P |
| 13832 | male | 5y | skeletal dysplasia | *COL2A1* | NM\_001844.4:c.3662C>T | p.(Ser1221Phe) | Homozygote; | F,M | LP |
| 13361 | female | 20m | skeletal dysplasia,facial dysmorphism,deafness,cheilopalatognathus | *COL2A1* | NM\_001844.4:c.905C>T | p.(Ala302Val) | Heterozygote | De novo | P |
| 13276 | male | 3y | skeletal dysplasia | *COL2A1* | NM\_001844.4:c.823C>T | p.(Arg275Cys) | Heterozygote | De novo | P |
| 10032 | male | 11y | skeletal dysplasia,facial dysmorphism | *COL3A1* | NM\_000090.3:c.574G>A | p.(Gly192Ser) | Heterozygote | De novo | LP |
| 13431 | male | 21m | skeletal dysplasia,developmental delay | *COL10A1* | NM\_000493.3:c.1765T>C | p.(Phe589Leu) | Heterozygote | M | LP |
| 13181 | male | 6y | skeletal dysplasia | *COL11A1* | NM\_001854.3:c.1245+1G>A | p.? | Heterozygote | F | LP |
| 2134 | female | 9y | skeletal dysplasia | *COMP* | NM\_000095.2:c.976G>A | p.(Asp326Asn) | Heterozygote | De novo | LP |
| 7541 | female | 10y | skeletal dysplasia | *COMP* | NM\_000095.2:c.1317C>G | p.(Asp439Glu) | Heterozygote | F | LP |
| 14121 | female | 1y2m | skeletal dysplasia | *COMP* | NM\_000095.2:c.1223A>G | p.(Asp408Gly) | Heterozygote | M | P |
| 8245 | male | 5y | skeletal dysplasia，CHD | *FBN1* | NM\_000138.4:c.5284G>A | p.(Gly1762Ser) | Heterozygote | De novo | P |
| 5621 | female | 15y | SGA,DSD,cheilopalatognathus,without olfactory bulb | *FGFR1* | NM\_023110.2:c.760C>T | p.(Arg254Trp) | Heterozygote | De novo | LP |
| 7151 | female | 14y | SGA,DSD | *FGFR1* | NM\_023110.2:c.1431-2A>C | p.? | Heterozygote | De novo | P |
| 3514 | female | 3y | skeletal dysplasia,facial dysmorphism,craniosynostosis | *FGFR2* | NM\_000141.4:c.1026C>G | p.(Cys342Trp) | Heterozygote | F | P |
| 10422 | female | 8 m | skeletal dysplasia,facial dysmorphism,hydrocephalus | *FGFR2* | NM\_000141.4:c.833G>T | p.(Cys278Phe) | Heterozygote | De novo | P |
| 5721 | male | 11 | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 6175 | female | 14 m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1620C>A | p.(Asn540Lys) | Heterozygote | De novo | P |
| 7197 | female | 12y | skeletal dysplasia,facial dysmorphism,SGA | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 7419 | male | 2y | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 7535 | female | 8 m | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 8305 | female | 3y | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 9049 | female | 8m | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1620C>G | p.(Asn540Lys) | Heterozygote | De novo | P |
| 8673 | female | 12y | skeletal dysplasia | *FGFR3* | NM\_000142.4: c.833A>G | p.(Tyr278Cys) | Heterozygote | De novo | LP |
| 10479 | female | 11y | skeletal dysplasia | *FGFR3* | NM\_000142.4: c.791C>T | p.(Thr264Met) | Heterozygote | M | P |
| 12585 | female | 8 m | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 13193 | male | 2y | skeletal dysplasia,facial dysmorphism,developmental delay | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 12696 | male | 11y | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1620C>A | p.(Asn540Lys) | Heterozygote | De novo | P |
| 13267 | male | 11y | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 13843 | female | 20 m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1620C>G | p.(Asn540Lys) | Heterozygote | De novo | P |
| 14365 | male | 12y6 m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1620C>G | p.(Asn540Lys) | Heterozygote | De novo | P |
| 11935 | female | 3m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | M | P |
| 12240 | female | 8y | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1620C>G | p.(Asn540Lys) | Heterozygote | De novo | P |
| 12249 | male | 9y | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1620C>A | p.(Asn540Lys) | Heterozygote | De novo | P |
| 2505 | male | 8 m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 1899 | male | 12y | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1620C>G | p.(Asn540Lys) | Heterozygote | De novo | P |
| 1969 | male | 10m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 2182 | male | 17 m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 3031 | female | 8y | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1620C>G | p.(Asn540Lys) | Heterozygote | De novo | P |
| 4230 | male | 3 m | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 4352 | male | 6m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 4554 | male | 3y | short stature | *FGFR3* | NM\_000142.4:c.1619A>G | p.(Asn540Ser) | Heterozygote | F | P |
| 5144 | male | 4m | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 5198 | male | 14y | skeletal dysplasia | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 5407 | male | 3y | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 5701 | female | 5y | skeletal dysplasia,facial dysmorphism | *FGFR3* | NM\_000142.4:c.1138G>A | p.(Gly380Arg) | Heterozygote | De novo | P |
| 11354 | female | 2y | skeletal dysplasia | *FGFR3,NPR2* | NM\_000142.4:c.1135T>C, (M);NM\_003995.3:c.2720C>T,(M); | FGFR3:p.(Tyr379His);NPR2:p.(Thr907Met) | Heterozygote;Heterozygote | M,M | LP,LP |
| 14081 | female | 8y | skeletal dysplasia | *NPR2* | NM\_003995.3:c.329del | p.(Arg110Profs\*11) | Heterozygote | M | P |
| 3863 | female | 5y | short stature | *IHH* | NM\_002181.3:c.797dup | p.(Arg267Thrfs\*15 ) | Heterozygote | F | LP |
| 5817 | female | 8y | skeletal dysplasia | *PTHLH* | NM\_198965.1:c.101+1G>C | p.? | Heterozygote | De novo | P |
| WJ-525 | female | 8y3m | facial dysmorphism,microcephaly, sensitive skin for sunshine | *BLM* | NM\_000057.3:[c.959+2T>A]/[c.772\_773del] | [p.?]/[p.(Leu258Glufs\*7)] | Compound heterozygote | F,M | P,P |
| 10616 | female | 11y | skeletal dysplasia,facial dysmorphism,microcephaly,primordial uterus,bleeding from the fundus | *ERCC6* | NM\_000124.3:[c.643G>T]/[c.1607T>G] | [p.(Glu215\*)]/[p.(Leu536Trp)] | Compound heterozygote | F,M | LP,LP |
| 3587 | male | 5y | anemia | *FANCE* | NM\_021922.2:c.1111C>T | p.(Arg371Trp) | Homozygote |  | P |
| 6712 | female | 10y | skeletal dysplasia,facial dysmorphism | *CUL7* | NM\_014780.4:[c.354delT]/[c.40delC] | [p.(Gln119Argfs\*52)]/[p.(Leu14Trpfs\*12)] | Compound heterozygote | F,M | P |
| 2040 | female | 2y | facial dysmorphism | *OBSL1* | NM\_015311.2:c.458dup | p.(Leu154Profs\*100) | Homozygote | F,M | LP |
| 7499 | female | 4y | skeletal dysplasia,facial dysmorphism | *OBSL1* | NM\_015311.2:c.458dup | p.(Leu154Profs\*100) | Homozygote | F,M | LP |
| 7724 | female | 5y | facial dysmorphism | *CHD7* | NM\_017780.3: c.6193C>T | p.(Arg2065Cys) | Heterozygote | De novo | LP |
| 12343 | male | 10y | small penis | *CHD7* | NM\_017780.3: c.5211-2A>G | p.? | Heterozygote | De novo | P |
| 4417 | male | 13y | facial dysmorphism | *CHD7* | NM\_017780.3:c.4964A>G | p.(Lys1655Arg) | Heterozygote | De novo | LP |
| 10868 | female | 5y | skeletal dysplasia,facial dysmorphism,developmental delay | *HDAC8* | NM\_018486.2: c.628+1G>C | p.? | Heterozygote | De novo | P |
| WJ-861 | male | 1y6m | facial dysmorphism | *NIPBL* | NM\_133433.3:c.6854\_6855del | p.(Gln2285Argfs\*3) | Heterozygote | De novo | P |
| 4734 | male | 10y | facial dysmorphism,cryptorchidism,CHD,intellectual disability | *NIPBL* | NM\_133433.3:c.3344G>A | p.(Trp1115\*) | Heterozygote | De novo | P |
| 7178 | male | 11y | facial dysmorphism,intellectual disability | *NIPBL* | NM\_133433.3:c.4422G>T | p.(Arg1474Ser) | Heterozygote | De novo | P |
| 7833 | male | 4y | facial dysmorphism,a freakish extra finger. | *NIPBL* | NM\_133433.3:c.7264-6T>G | p.? | Heterozygote | De novo | LP |
| 9838 | female | 2y | facial dysmorphism,developmental delay | *NIPBL* | NM\_133433.3:c.330\_331del | p.(Ser111Hisfs\*16) | Heterozygote | De novo | P |
| 11213 | female | 4y | facial dysmorphism,developmental delay,finger deformities | *NIPBL* | NM\_133433.3:c.-79-2A>G | p.? | Heterozygote | De novo | LP |
| 10475 | male | 4y | facial dysmorphism,microcephaly, developmental delay | *SMC1A* | NM\_006306.3:c.1088G>T | p.(Arg363Ile) | Heterozygote | De novo | LP |
| 12723 | female | 2y | facial dysmorphism,developmental delay | *SMC3* | NM\_005445.3:c.95G>A | p.(Gly32Asp) | Heterozygote | De novo | LP |
| 10635 | male | 4y | skeletal dysplasia,facial dysmorphism | *LMNA* | NM\_170707.3:c.433G>A | p.(Glu145Lys) | Heterozygote | De novo | P |
| WJ-584(2066) | male | 11y | facial dysmorphism,ear deformities,small testes,SGA | *ORC6* | NM\_014321.3:c.67A>G | p.(Lys23Glu) | Homozygote | F,M | LP |
| WJ-656(2258) | male | 13y | facial dysmorphism,microcephaly,intellectual disability,SGA | *PCNT* | NM\_006031.5:[c.3103C>T]/[c.502C>T] | [p.(Arg1035\*)]/[p.(Gln168\*)] | Compound heterozygote | F,M | LP,LP |
| 6556 | female | 7y | facial dysmorphism,intellectual disability | *KDM6A* | NM\_021140.3:c.1834C>T | p.(Arg612\* ) | Heterozygote | De novo | P |
| 7933 | male | 5y | developmental delay | *KDM6A* | NM\_021140.3:c.404G>A | p.(Gly135Asp) | Heterozygote | De novo | LP |
| 6983 | female | 43天 | hypoglycemia | *KMT2D* | NM\_003482.3:c.16018C>T | p.(Arg5340\* ) | Heterozygote | De novo | P |
| 11639 | female | 4 m | facial dysmorphism | *KMT2D* | NM\_003482.3:c.15163\_15168del | p.(Asp5055\_Leu5056del) | Heterozygote | De novo | P |
| 14242 | male | 8y | facial dysmorphism,intellectual disability | *KMT2D* | NM\_003482.3:c.11839C>T | p.(Gln3947\* ) | Heterozygote | De novo | P |
| 6230 | male | 9y | skeletal dysplasia | *ANKRD11* | NM\_013275.5:c.6982dup | p.(Arg2328Profs\*204 ) | Heterozygote | De novo | P |
| 8816 | male | 4y | CHD,SGA | *ANKRD11* | NM\_013275.5:c.3140\_3143del | p.(Gln1047Argfs\*270 ) | Heterozygote | M | LP |
| 12210 | male | 17y | CHD,intellectual disability | *ANKRD11* | NM\_013275.5:c.7569+1G>C | p.? | Heterozygote | De novo | LP |
| 11966 | male | 8y | facial dysmorphism,intellectual disability | *ANKRD11* | NM\_013275.5:c.7237C>T | p.(Gln2413\* ) | Heterozygote | De novo | P |
| 4487 | female | 7y | facial dysmorphism,intellectual disability | *CREBBP* | NM\_004380.2:c.1775G>A | p.(Trp592\*) | Heterozygote | De novo | P |
| 9125 | male | 3y11m | facial dysmorphism,developmental delay,cryptorchidism | *CREBBP* | NM\_004380.2:c.2881-13G>A | p.? | Heterozygote | De novo | LP |
| 4830 | male | 4y | cleft lip and palate | *SHOX* | NM\_000451.3:c.526G>T | p.(Glu176\*) | Heterozygote | De novo | LP |
| 11457 | male | 2y | skeletal dysplasia | *SHOX* | NM\_000451.3:c.283dupT | p.(Tyr95Leufs\*2) | Heterozygote | F | LP |
| 13343 | female | 7y | skeletal dysplasia | *SHOX* | deletion (whole gene) |  |  |  | P |
| 8895 | female | 12y | skeletal dysplasia | *SHOX* | deletion (whole gene) |  |  |  | P |
| 5558 | male | 8y | cryptorchidism | *SOX11* | NM\_003108.3:c.337T>C | p.(Tyr113His) | Heterozygote | De novo | LP |
| 7500 | male | 3y | SGA | *SOX11* | NM\_003108.3:c.425C>G | p.(Ala142Gly) | Heterozygote | De novo | LP |
| 4213 | male | 2y | facial dysmorphism | *KMT2A* | NM\_001197104.1:c.10752dup | p.(Gly3585Argfs\*8) | Heterozygote | De novo | P |
| 5341 | female | 5y | facial dysmorphism,developmental delay,SGA,CHD | *KMT2A* | NM\_001197104.1:c.11716C>T | p.(Arg3906Cys) | Heterozygote | De novo | LP |
| 6436 | female | 9y | short stature | *KMT2A* | NM\_001197104.1:c.3241C>T | p.(Arg1081\*) | Heterozygote | De novo | P |
| 6557 | male | 6y | facial dysmorphism | *KMT2A* | NM\_001197104.1:c.5871T>A | p.(Tyr1957\*) | Heterozygote | De novo | P |
| 8569 | female | 7y | short stature | *KMT2A* | NM\_001197104.1:c.7371del | p.(Gly2458Valfs\*6) | Heterozygote | De novo | P |
| 8304 | male | 13y | intellectual disability | *KMT2A* | NM\_001197104.1:c.3241C>T | p.(Arg1081\*) | Heterozygote | De novo | P |
| 10589 | male | 5y | developmental delay,cryptorchidism, hairy elbows | *KMT2A* | NM\_005933.3:c.3460C>T | p.(Arg1154Trp) | Heterozygote | De novo | P |
| 10925 | male | 11m | developmental delay | *KMT2A* | NM\_001197104.1:c.3461\_3473del | p.(Arg1154Leufs\*17) | Heterozygote | De novo | P |
| 11344 | male | 10y | intellectual disability,strabismus | *KMT2A* | NM\_001197104.1:c.4086+2T>G | p.? | Heterozygote | De novo | P |
| 11962 | female | 3y | short stature,hairy elbows | *KMT2A* | NM\_001197104.1:c.7849del | p.(Arg2617Glyfs\*24) | Heterozygote | De novo | P |
| 2822 | female | 2y5 m | skeletal dysplasia | *GNAS* | NM\_000516.4:c.212+3\_212+6delAAGT | p.? | Heterozygote | M | LP |
| 4103 | female | 12y | skeletal dysplasia | *GNAS* | NM\_000516.4:c.314C>T | p.(Thr105Ile) | Heterozygote | De novo | LP |
| 4881 | female | 14y | primordial uterus,gonadal dysplasia | *GNAS* | NM\_000516.4: c.1006C>T | p.(Arg336Trp) | Heterozygote | De novo | LP |
| 6562 | male | 10y | short stature | *GNAS* | NM\_000516.4:c.308T>C | p.(Ile103Thr) | Heterozygote | De novo | P |
| 7246 | male | 11y | skeletal dysplasia | *GNAS* | NM\_000516.4:c.565\_568del | p.(Asp189Metfs\*14) | Heterozygote | M | P |
| 12628 | female | 11y3 m | skeletal dysplasia | *GNAS* | NM\_000516.5:c.308T>C | p.(Ile103Thr) | Heterozygote | De novo | P |
| 7780 | male | 3 m | facial dysmorphism,skeletal dysplasia,developmental delay | *FAM111A* | NM\_022074.3:c.1706G>A | p.(Arg569His) | Heterozygote | De novo | P |
| 6522 | male | 5y | facial dysmorphism,developmental delay,langerhans cell histiocytosis | *MAP2K1* | NM\_002755.3:c.161T>C | p.(Leu54Pro) | Heterozygote | De novo | LP |
| 6891 | male | 5y | developmental delay,cryptorchidism, | *MAP2K1* | NM\_002755.3:c.389A>G | p.(Tyr130Cys) | Heterozygote | De novo | P |
| 7015 | female | 8y | facial dysmorphism,skeletal dysplasia,intellectual disability,clubfoot | *HRAS* | NM\_005343.2:c.34G>A | p.(Gly12Ser) | Heterozygote | De novo | P |
| 2541 | male | 4y | developmental delay | *KAT6B* | NM\_012330.3:c.2636T>A | p.(Leu879\*） | Heterozygote | De novo | P |
| 9948 | male | 13 m | facial dysmorphism,developmental delay | *KAT6B* | NM\_012330.3:c.3405dup | p.(Lys1136\*) | Heterozygote | De novo | P |
| 3221 | female | 4y | CHD | *NF1* | NM\_000267.3:c.281T>C | p.(Leu94Pro) | Heterozygote | M | LP |
| 3985 | female | 4y | skeletal dysplasia,caf-au-lait spots | *NF1* | NM\_000267.3:c.3445A>G | p.(Met1149Val) | Heterozygote | De novo | P |
| 4100 | male | 7y | caf-au-lait spots | *NF1* | NM\_000267.3:c.1541\_1542del | p.(Gln514Argfs\*43) | Heterozygote | De novo | P |
| 4837 | female | 7y | skeletal dysplasia,caf-au-lait spots | *NF1* | NM\_000267.3: c.3256C>T | p.(Gln1086\*) | Heterozygote | De novo | P |
| 5671 | female | 4y | caf-au-lait spots | *NF1* | NM\_000267.3: c.4180A>C | p.(Asn1394His) | Heterozygote | De novo | LP |
| 5683 | male | 11y | caf-au-lait spots | *NF1* | NM\_000267.3c.4469T>C | p.(Leu1490Pro) | Heterozygote | M | LP |
| 7824 | male | 2y | caf-au-lait spots | *NF1* | NM\_000267.3:c.1586T>C | p.(Leu529Pro) | Heterozygote | M | P |
| 8633 | female | 4y | caf-au-lait spots | *NF1* | NM\_000267.3:c.5605G>C | p.(Gly1869Arg) | Heterozygote | De novo | LP |
| 9077 | female | 11y | myopia,astigmatism,caf-au-lait spots | *NF1* | NM\_000267.3:c.6792C>A | p.(Tyr2264\*) | Heterozygote | De novo | P |
| 9127 | male | 13y | caf-au-lait spots | *NF1* | NM\_000267.3:c.5749+1G>A | p.? | Heterozygote | F | P |
| 13983 | male | 7y | caf-au-lait spots | *NF1* | NM\_000267.3:c.6789\_6792del | p.(Tyr2264Thrfs\*5) | Heterozygote | De novo | P |
| 13815 | male | 12y | caf-au-lait spots | *NF1* | NM\_000267.3:c.3610C>T | p.(Arg1204Trp) | Heterozygote | F | P |
| 11564 | female | 9y | caf-au-lait spots | *NF1* | NM\_000267.3:c.4267A>G | p.(Lys1423Glu) | Heterozygote | De novo | P |
| 12945 | male | 12y | facial dysmorphism,intellectual disability | *BRAF* | NM\_004333.5:c.739T>C | p.(Phe247Leu) | Heterozygote | De novo | LP |
| 9097 | male | 11y | facial dysmorphism,skeletal dysplasia,hyperopia,CHD | *KRAS* | NM\_004985.4:c.458A>T | p.(Asp153Val) | Heterozygote | De novo | P |
| 3745 | male | 2y | facial dysmorphism,skeletal dysplasia,CHD | *PTPN11* | NM\_002834.3:c.1510A>G | p.(Met504Val) | Heterozygote | De novo | P |
| 4350 | female | 10y | facial dysmorphism,skeletal dysplasia,CHD | *PTPN11* | NM\_002834.3:c.1510A>G | p.(Met504Val) | Heterozygote |  | P |
| 5657 | male | 10y | facial dysmorphism,skeletal dysplasia,cryptorchidism | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| 6758 | female | 5y | facial dysmorphism | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote |  | P |
| 8953 | male | 11y | facial dysmorphism,skeletal dysplasia,cryptorchidism,CHD | *PTPN11* | NM\_002834.3:c.923A＞G | p.(Asn308Ser) | Heterozygote | M | P |
| 8394 | female | 8y | facial dysmorphism,skeletal dysplasia,amblyopia,astigmatism,deafness | *PTPN11* | NM\_002834.3:c.218C>T | p.(Thr73Ile) | Heterozygote | De novo | P |
| 8491 | male | 7y | facial dysmorphism,skeletal dysplasia,intellectual disability,astigmatism | *PTPN11* | NM\_002834.3:c.1492C>T | p.(Arg498Trp) | Heterozygote | F | P |
| 8591 | female | 12y | GHI,CHD | *PTPN11* | NM\_002834.3:c.188A>G | p.(Tyr63Cys) | Heterozygote | De novo | P |
| 8823 | female | 13y | GHI | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| 8824 | female | 13y | GHI | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| 5465 | male | 7y | facial dysmorphism,skeletal dysplasia,cryptorchidism | *PTPN11* | NM\_002834.3:c.182A>G | p.(Asp61Gly） | Heterozygote | De novo | P |
| 9217 | male | 11y | skeletal dysplasia,CHD | *PTPN11* | NM\_002834.4:c.181G>A | p.(Asp61Asn) | Heterozygote | De novo | P |
| 9371 | female | 4y | facial dysmorphism,deafness | *PTPN11* | NM\_002834.4:c.417G>C | p.(Glu139Asp) | Heterozygote | De novo | P |
| 10342 | female | 12y | facial dysmorphism,skeletal dysplasia,amblyopia,CHD | *PTPN11* | NM\_002834.4:c.181G>A | p.(Asp61Asn) | Heterozygote | De novo | P |
| 10482 | male | 7y | facial dysmorphism,skeletal dysplasia,cryptorchidism,CHD | *PTPN11* | NM\_002834.4:c.1472C>A | p.(Pro491His) | Heterozygote | De novo | P |
| 10534 | female | 11y | facial dysmorphism,skeletal dysplasia,CHD | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| 14222 | male | 6 m | facial dysmorphism,CHD,cryptorchidism | *PTPN11* | NM\_002834.3:c.215C>G | p.(Ala72Gly) | Heterozygote | De novo | P |
| 13282 | male | 9y | CHD | *PTPN11* | NM\_002834.4:c.184T>G | p.(Tyr62Asp) | Heterozygote | De novo | P |
| 13477 | male | 5y10 m | cryptorchidism | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| 11149 | male | 13y | facial dysmorphism,deafness | *PTPN11* | NM\_002834.4:c.1502G>A | p.(Arg501Lys) | Heterozygote | De novo | LP |
| 11855 | female | 5y | facial dysmorphism,CHD | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| 11825 | male | 11y | facial dysmorphism | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| 10892 | male | 7y | facial dysmorphism,CHD,cryptorchidism,GHI,caf-au-lait spots | *PTPN11* | NM\_002834.3:c.922A>G | p.(Asn308Asp) | Heterozygote | De novo | P |
| ＊ | male | 8y | CHD,GHI | *PTPN11* | NM\_002834.3:c.844A＞G | p.(Ile282Val) | Heterozygote | De novo | P |
| 8637 | female | 7y | facial dysmorphism,CHD,intellectual disability | *RAF1* | NM\_002880.3:c.786T>G | p.(Asn262Lys) | Heterozygote | De novo | P |
| 8708 | male | 11y | facial dysmorphism,skeletal dysplasia,intellectual disability,cryptorchidism,CHD | *RAF1* | NM\_002880.3:c.1837C>G | p.(Leu613Val) | Heterozygote | De novo | P |
| 11157 | female | 4y | facial dysmorphism,CHD | *RIT1* | NM\_006912.5:c.67A>C | p.(Lys23Gln) | Heterozygote | De novo | LP |
| WJ-862 | male | 3y | facial dysmorphism,skeletal dysplasia,CHD | *SHOC2* | NM\_007373.3:c.4A>G | p.(Ser2Gly) | Heterozygote | De novo | P |
| 12429 | male | 12y | CHD | *SHOC2* | NM\_007373.3:c.4A>G | p.(Ser2Gly) | Heterozygote | De novo | P |
| 6896 | female | 6y | facial dysmorphism,skeletal dysplasia,CHD,amblyopia,strabismus | *SOS1* | NM\_005633.3:c.1656G>T | p.(Arg552Ser) | Heterozygote | De novo | P |
| 6944 | male | 5 m | facial dysmorphism,cryptorchidism,CHD | *SOS1* | NM\_005633.3:c.1655G>A | p.(Arg552Lys) | Heterozygote | De novo | P |
| 5001 | female | 7y | skeletal dysplasia,intellectual disability | *CLCN7* | NM\_001287.5:c.896C>T | p.(Ala299Val) | Heterozygote | De novo | P |
| 11795 | female | 3y9 m | skeletal dysplasia,nystagmus | *CLCN7* | NM\_001287.5:c.857G>A | p.(Arg286Gln) | Heterozygote | F | LP |
| 13779 | female | 3y | skeletal dysplasia | *TCIRG1* | NM\_006019.3:[c.117+5G>A]/[c.2236+6T>G] | [p.?]/[p.?] | Compound heterozygote | F,M | LP,LP |
| 2975 | male | 11y | skeletal dysplasia | *EXT1* | NM\_000127.2:c.2098C>T | p.(Gln700\*) | Heterozygote | De novo | P |
| 4111 | male | 10y | skeletal dysplasia | *EXT1* | NM\_000127.2:c.1431dup | p.(Ser478Leufs\*43) | Heterozygote | De novo | P |
| 9162 | male | 10y | skeletal dysplasia | *EXT1* | NM\_000127.2:c.1154T>A | p.(Leu385\*) | Heterozygote | F | P |
| 10426 | female | 4y | skeletal dysplasia | *EXT1* | NM\_000127.2:c.1836G>A | p.(Trp612\*) | Heterozygote | De novo | P |
| 10346 | female | 8y | congenital hypothyroidism | *DUOX2* | NM\_014080.4:c.1462G>A | p.(Gly488Arg) | Homozygote; | M | LP |
| 2221 | male | 12y | congenital hypothyroidism | *DUOX2* | NM\_014080.4:[c.3329G>A]/[c.1310G>C] | [p.(Arg1110Gln)]/[p.(Gly437Ala)] | Compound heterozygote | F,M | LP,LP |
| 8911 | male | 13 m | facial dysmorphism,convulsions | *PAX3* | NM\_181457.3:c.811C>T | p.(Arg271Cys) | Heterozygote | M | LP |
| 8894 | male | 9y | small testicles,congenital hypothyroidism | *PAX8* | NM\_003466.3:c.92G>A | p.(Arg31His) | Heterozygote | De novo | LP |
| 8903 | male | 13y5 m | facial dysmorphism,congenital hypothyroidism | *THRA* | NM\_199334.3:c.802G>A | p.(Asp268Asn) | Heterozygote | De novo | LP |
| 13050 | female | 18y | facial dysmorphism,nystagmus,skeletal dysplasia,congenital hypothyroidism | *TPO* | NM\_000547.5:[c.977C>T]/[c.670\_672del] | [p.(Ala326Val)]/[p.(Asp224del)] | Compound heterozygote | F,M | LP,LP |
| 5866 | female | 8y | congenital hypothyroidism | *TSHR* | NM\_000369.2:[c.394G>C]/[c.1556G>A] | [p.(Gly132Arg)]/[p.(Arg519His)] | Compound heterozygote | F,M | LP,LP |
| 9328 | female | 2y | skeletal dysplasia | *ARSB* | NM\_000046.4:[c.1197C>G]/[c.943C>T] | [p.(Phe399Leu)]/[p.(Arg315\*)] | Compound heterozygote | F,M | LP,P |
| 9887 | male | 8y | facial dysmorphism,skeletal dysplasia | *ARSB* | NM\_000046.4:[c.200T>G]/[c.342C>G]/[c.475C>T] | [p.(Ile67Ser)]/[p.(Ile114Met)]/[p.(Arg159Cys)] | Compound heterozygote | F,M,M | LP,LP,LP |
| 6479 | male | 14 m | hepatic insufficiency | *G6PC* | NM\_000151.3:[c.648G>T]/[c.248G>A] | [p.(Leu216Leu)]/[p.(Arg83His)] | Compound heterozygote | F,M | LP,LP |
| 9581 | female | 19 m | facial dysmorphism,skeletal dysplasia,CHD | *GNPTAB* | NM\_024312.4:c.1090C>T | p.(Arg364\*) | Homozygote; | F,M | P |
| 12021 | male | 8y | facial dysmorphism,skeletal dysplasia | *GNPTAB* | NM\_024312.4:c.[1284+1G>T]/[1307C>T] | [p.?]/[p.(Pro436Leu)] | Compound heterozygote | F,M | LP,LP |
| 9669 | male | 9y | facial dysmorphism,skeletal dysplasia | *GUSB* | NM\_000181.3:c.[1244+3G>C]/[1324G>A] | [p.?]/[p.(Ala442Thr)] | Compound heterozygote | F,M | LP,LP |
| 3549 | male | 5y | facial dysmorphism,skeletal dysplasia | *IDS* | NM\_000202.6:c.1006+2T>G | p.? | Heterozygote | M | LP |
| 3992 | male | 12y | skeletal dysplasia | *IDS* | NM\_000202.6:c.1037C>T | p.(Ala346Val) | Heterozygote | M | LP |
| 6607 | male | 6y | facial dysmorphism,skeletal dysplasia | *IDS* | NM\_000202.6:c.240+1G>A | p.? | Heterozygote | M | P |
| 8940 | male | 5y | facial dysmorphism,skeletal dysplasia,CHD | *IDS* | NM\_000202.6:c.820dup | p.(Glu274Glyfs\*68) | Heterozygote | M | P |
| 8976 | female | 10y | skeletal dysplasia | *IDS* | NM\_000202.6:c.182C>T | p.(Ser61Phe) | Heterozygote | M | LP |
| 9761 | male | 6y | facial dysmorphism,skeletal dysplasia,intellectual disability | *IDS* | NM\_000202.6:c.943\_944dup | p.(Leu315Phefs\*2) | Heterozygote | M | P |
| 13423 | male | 6y | facial dysmorphism,skeletal dysplasia | *IDS* | NM\_000202.6:c.507+1G>A | p.? | Heterozygote | M | P |
| 11189 | male | 5y | skeletal dysplasia | *IDS* | NM\_000202.6:c.182C>T | p.(Ser61Phe) | Heterozygote | M | LP |
| 11979 | male | 2y | skeletal dysplasia,CHD | *IDS* | NM\_000202.6:[Exon 9 del] | p.? |  |  | P |
| 6759 | male | 4y | hepatic insufficiency,intellectual disability | *PHKA2* | NM\_000292.2:c.1459+1G>A | p.? | Heterozygote | M | LP |
| 13555 | female | 13y9 m | skeletal dysplasia,intellectual disability | *SGSH* | NM\_000199.4:c.962C>A | p.(Thr321Asn) | Homozygote; | F,M | LP |
| 11072 | male | 15y | gynandrism | *AR* | NM\_000044.4:c.2113C>T | p.(Leu705Phe) | Heterozygote | M | LP |
| 14304 | male | 2y | microcephaly,intellectual disability | *ATP6V1B1* | NM\_001692.4:[c.370C>T]/[c.1397C>A] | [p.(Arg124Trp)]/[p.(Ser466\*)] | Heterozygote | F,M | P,LP |
| 4743 | female | 9y | hypophosphatemia | *CASR* | NM\_000388.3:c.3082C>T | p.(Gln1028\*) | Heterozygote | M | LP |
| 2671 | male | 12y | short stature | *CASR* | NM\_000388.3:c.2405A>T | p.(Asn802Ile) | Heterozygote | De novo | P |
| 9153 | female | 3y11m | SGA | *CASR* | NM\_000388.3:c.897G>A | p.(Trp299\*) | Heterozygote | F | LP |
| 10775 | male | 3y2 m | skeletal dysplasia | *CYP27B1* | NM\_000785.3:[c.1165C>T]/[c.589+1G>A] | [p.(Arg389Cys)]/[p.?] | Compound heterozygote | F,M | P,P |
| 12496 | male | 3y | skeletal dysplasia | *FLNA* | NM\_001456.3:c.3527G>A | p.(Gly1176Glu) | Heterozygote | De novo | LP |
| 13184 | female | 3y | skeletal dysplasia | *FLNB* | NM\_001457.3:c.4241del | p.(Pro1414Leufs\*2) | Heterozygote | F | LP |
| 10666 | male | 5y | deafness | *GJB2* | NM\_004004.5:[c.235del]/[c.109G>A] | [p.(Leu79Cysfs\*3)]/[p.(Val37Ile)] | Compound heterozygote | F,M | P,P |
| 11897 | male | 4y | deafness | *GJB2* | NM\_004004.5:c.235del | p.(Leu79Cysfs\*3) | Homozygote; | F,M | P |
| 9444 | female | 7y4 m | intellectual disability | *GRIN1* | NM\_007327.3:c.1852G>A | p.(Gly618Ser) | Heterozygote | De novo | LP |
| 13165 | female | 11y | intellectual disability,GHI,spina bifida | *KMT2C* | NM\_170606.3:c.3841+1G>A | p.? | Heterozygote | De novo | LP |
| 6872 | male | 8y | facial dysmorphism,skeletal dysplasia | *LMX1B* | NM\_002316.3:c.248G>T | p.(Cys83Phe) | Heterozygote | De novo | P |
| 3573 | male | 9y | intellectual disability,congenital strabismus | *MED12* | NM\_005120.2:c.887G>C | p.(Arg296Pro) | Heterozygote | M | LP |
| 8071 | male | 6y | intellectual disability | *MED12* | NM\_005120.2:c.2881C>T | p.(Arg961Trp) | Heterozygote | M | P |
| 8821 | male | 12y | skeletal dysplasia,intellectual disability | *MFN2* | NM\_014874.3:c.384C>A | p.(His128Gln) | Heterozygote | De novo | LP |
| 8229 | male | 12y | facial dysmorphism,skeletal dysplasia | *NOTCH2* | NM\_024408.3:c.6449\_6450del | p.(Pro2150Argfs\*2) | Heterozygote | De novo | P |
| 7311 | male | 7 m | facial dysmorphism,skeletal dysplasia,developmental delay | *OFD1* | NM\_003611.2:c.2del | p.? | Heterozygote | M | LP |
| 2867 | male | 19 m | skeletal dysplasia | *OFD1* | NM\_003611.2:c.2590C>T | p.(Gln864\*) | Heterozygote | M | LP |
| 2791 | male | 7y | skeletal dysplasia, hypophosphatemia | *PHEX* | NM\_000444.5:c.1960\_1965+2dupTTTAGGGT | p.? | Heterozygote | De novo | P |
| 6386 | female | 3y | skeletal dysplasia | *PHEX* | NM\_000444.5:[Exon 1-5 del] | p.? | Heterozygote | De novo | P |
| 8828 | female | 4y | skeletal dysplasia | *PHEX* | NM\_000444.5:[Exon 13 del] | p.? | Heterozygote |  | LP |
| 8926 | female | 4y | skeletal dysplasia | *PHEX* | NM\_000444.5:c.2147+1\_2147+2delinsAGGGGC | p.? | Heterozygote | M | LP |
| 6824 | female | 5y | skeletal dysplasia | *PHEX* | NM\_000444.5:c.1971C>A | p.(Tyr657\*) | Heterozygote | De novo | P |
| 7398 | male | 6y | skeletal dysplasia | *PHEX* | NM\_000444.5:c.776T>C | p.(Leu259Pro) | Heterozygote | M | LP |
| 7404 | male | 6 m | skeletal dysplasia | *PHEX* | NM\_000444.5:c.1601C>T | p.(Pro534Leu) | Heterozygote | M | P |
| 7761 | female | 13y | skeletal dysplasia | *PHEX* | NM\_000444.5:c.733-1G>A | p.? | Heterozygote | De novo | P |
| 8492 | female | 10y | skeletal dysplasia | *PHEX* | NM\_000444.5:c.1971C>G | p.(Tyr657\*) | Heterozygote | M | P |
| 12638 | female | 6y | skeletal dysplasia | *PHEX* | NM\_000444.5:c.350-1G>T | p.? | Heterozygote |  | P |
| 11777 | female | 3y | skeletal dysplasia | *PHEX* | NM\_000444.5:c.1735G>A | p.(Gly579Arg) | Heterozygote | de novo | P |
| 8524 | female | 18 m | developmental delay | *POGZ* | NM\_015100.3:c.3847C>T | p.(Gln1283\*) | Heterozygote | De novo | LP |
| 8987 | female | 9y | facial dysmorphism,intellectual disability | *POGZ* | NM\_015100.3:c.2310C>G | p.(Tyr770\*) | Heterozygote | De novo | LP |
| 7387 | female | 9y | intellectual disability | *MECP2* | NM\_004992.3:[Exon 2-3 del] | p.? | Heterozygote | De novo | P |
| 10505 | female | 2y3 m | developmental delay | *MECP2* | NM\_004992.3:c.905C>T | p.(Pro302Leu) | Heterozygote | De novo | P |
| 5867 | male | 14y | skeletal dysplasia | *RUNX2* | NM\_001024630.3:c.912delC | p.(Ser305Profs\*3) | Heterozygote | De novo | P |
| 7950 | male | 3y | skeletal dysplasia | *RUNX2* | NM\_001024630.3:c.606delC | p.(Val203Serfs\*8) | Heterozygote | De novo | P |
| 8044 | female | 2y | skeletal dysplasia | *RUNX2* | NM\_001024630.3:c.674G>A | p.(Arg225Gln) | Heterozygote | De novo | P |
| 13439 | male | 3 m | skeletal dysplasia | *RUNX2* | NM\_001024630.3:c.673C>T | p.(Arg225Trp) | Heterozygote | De novo | P |
| 13700 | female | 5 m | hypokalemia,diabetes insipidus,sponge kidney degeneration | *SLC12A1* | NM\_000338.2:[c.2711delA]/[c.3096+1G>A] | [p.(Lys904Argfs\*19)]/[p.?] | Compound heterozygote | F/M | P,P |
| 5722 | male | 13y | gonadal dysplasia | *SLC12A3* | NM\_000339.2:[c.965-1\_976delinsACCGAAAATTTT]/[c.1456G>A] | [p.?]/[p.(Asp486Asn)] | Compound heterozygote | F/M | P,P |
| 11249 | male | 7y | hypokalemia,internal organs reverse | *SLC12A3* | NM\_000339.2:[c.836T>G]/[c.602-16G>A] | [p.(Met279Arg)]/[p.?] | Compound heterozygote | F/M | LP,LP |
| 10972 | male | 5y | hypokalemia | *SLC12A3* | NM\_000339.2:[c.2877\_2878delAG]/[c.179C>T] | [p.(Arg959Serfs\*11)]/[p.(Thr60Met)] | Compound heterozygote | F/M | P,P |
| 12583 | female | 13y | hypokalemia | *SLC12A3* | NM\_000339.2:[c.179C>T]/[c.533C>T] | [p.(Thr60Met)]/[p.(Ser178Leu)] | Compound heterozygote | M/? | P,P |
| 12760 | female | 6y | hypokalemia | *SLC12A3* | NM\_000339.2:[c.911C>T]/[c.1445G>A] | [p.(Thr304Met)]/[(p.Cys482Tyr)] | Compound heterozygote | F/M | LP,LP |
| 13591 | male | 9y | hypokalemia,hypomagnesemia,spina bifida | *SLC12A3* | NM\_000339.2:c.1679C>A | p.(Pro560His) | Homozygote; | F/M | LP |
| 3254 | male | 3y | skeletal dysplasia | *TRPS1* | NM\_014112.4:c.2657C>A | p.(Ser886\*) | Heterozygote | M | LP |
| 5836 | male | 10y | skeletal dysplasia | *TRPS1* | NM\_014112.4:c.2762G>A | p.(Arg921Gln) | Heterozygote | F | LP |
| 6428 | male | 2y | skeletal dysplasia | *TRPV4* | NM\_021625.4:c.1781G>A | p.(Arg594His) | Heterozygote | De novo | P |
| 12639 | female | 4y | skeletal dysplasia | *TRPV4* | NM\_021625.4:c.1780C>A | p.(Arg594Ser) | Heterozygote | De novo | P |
| 5862 | male | 13y | skeletal dysplasia | *WISP3* | NM\_003880.3:c.667T>C | p.(Cys223Arg) | Homozygote; | F/M | LP |
| 2378 | male | 14y | congenital hypospadias,cryptorchidism,polydactyly,cystic kidney disease,impaired vision,,intellectual disability | *BBS2* | NM\_031885.3:c.1148\_1149dup | p.(His384Serfs\*34) | Homozygote; | F/M | P |
| 12377 | male | 10y | skeletal dysplasia | *GALNS* | NM\_000512.4:[c.775C>T]/[c.245C>T] | [p.(Arg259Trp)]/[p.(Ser82Leu)] | Compound heterozygote | F/M | LP,LP |
| 2568 | male | 2y | skeletal dysplasia | *GALNS* | NM\_000512.4:[c.106\_111del]/[c.812T>C] | [p.(Leu36\_Leu37del)]/[p.(Leu271Pro)] | Compound heterozygote | F/M | P,LP |
| 2574 | male | 10y | facial dysmorphism,skeletal dysplasia,abnormal liver function | *NBAS* | NM\_015909.3:[c.500\_501del]/[c.5752A>C] | [p.(Phe167Cysfs\*7)]/[p.(Thr1918Pro)] | Compound heterozygote | F/M | LP,LP |
| 2896 | female | 4y | facial dysmorphism | *TFAP2A* | NM\_003220.2:c.202C>T | p.(Gln68\*) | Heterozygote | De novo | P |
| 3969 | male | 12y | MPHD,microscopic hematuria | *NPHP4* | NM\_015102.4:c.3196C>T | p.(Gln1066\*) | Homozygote | F/M | P |
| 4582 | male | 13y | congenital hyperlipidemia,polytrichia | *GPD1* | NM\_005276.3:[c.220-2A>G]/[c.820G>A] | [p.?]/[p.(Ala274Thr)] | Compound heterozygote | F/M | LP,LP |
| 4774 | male | 35d | CHD, cryptorchidism | *PEX26* | NM\_017929.5:[c.354delC]/[c.34del] | [p.(Val120Serfs\*61)]/[p.(Leu12Serfs\*70)] | Compound heterozygote | F/M | P,P |
| 6701 | female | 1 m | facial dysmorphism,skeletal dysplasia | *EFNB1* | NM\_004429.4:c.196C>T | p.(Arg66\*) | Heterozygote | De novo | P |
| 7290 | male | 4y | SGA | *RPS7* | NM\_021140.3:c.75+2T>C | p.? | Heterozygote |  | LP |
| 8061 | male | 7y10 m | skeletal dysplasia | *AMER1* | NM\_152424.3:c.301G>T | p.(Glu101\*) | Heterozygote | M | LP |
| 8086 | male | 3y | developmental delay | *KDM5C* | NM\_004187.3:c.4402G>T | p.(Glu1468\*) | Heterozygote | De novo | P |
| 9021 | male | 7y | facial dysmorphism,SGA | *POC1A* | NM\_015426.4:c.981+1G>A | p.? | Homozygote; | F/M | P |
| 6746 | female | 2y | facial dysmorphism | *GJA1* | NM\_000165.4:c.715C>T | p.(Arg239Trp) | Heterozygote | De novo | LP |
| 12978 | male | 5y | skeletal dysplasia | *SBDS* | NM\_016038.3:c.258+2T>C | p.? | Homozygote; | F/M | P |
| 14317 | male | 12y8 m | small testicles,small penis | *SOX2* | NM\_003106.3:c.259A>G | p.(Lys87Glu) | Heterozygote | De novo | LP |
| 12004 | male | 11y | skeletal dysplasia | *TRAPPC2* | NM\_001011658.3:c.271\_275del | p.(Gln91Argfs\*9) | Heterozygote | M | P |
| 12446 | male | 8y | facial dysmorphism,skeletal dysplasia,intellectual disability | *TWIST1* | NM\_000474.3:c.309C>G | p.(Tyr103\*) | Heterozygote | M | LP |
| 13099 | male | 15 m | CHD | del(22)(q11.21)[hg19(chr22:18,900,287-21,245,501)]  (over 2300kb) | | | | | P |
| 12594 | male | 14 m | facial dysmorphism,CHD,  cleft lip and palate | del(22)(q11.21)[hg19(chr22:18,900,287-21,245,501)]  (over 2300kb) | | | | | P |
| 10499 | male | 15y | facial dysmorphism,CHD | del(22)(q11.21)[hg19(chr22:18,900,287-21,245,501)]  (over 2300kb) | | | | | P |
| 9260 | female | 3y10 m | skeletal dysplasia,CHD,developmental delay | del(22)(q11.21)[hg19(chr22:18,900,287-21,245,501)]  (over 2300kb) | | | | | P |
| 8141 | female | 6y | facial dysmorphism,intellectual disability,cleft lip and palate | del(22)(q11.21)[hg19(chr22:18,900,287-21,245,501)] (  over 2300kb) | | | | | P |
| 7611 | male | 8y | CHD | del(22)(q11.21)[hg19(chr22:18,900,287-21,245,501)]  (over 2300kb) | | | | | P |
| 3691 | male | 12y | intellectual disability | del(22)(q11.21)[hg19(chr22:18,910,683-21,461,788)] (2551kb) | | | | | P |
| 5428 | male | 12y | intellectual disability,CHD | del(7)(q11.23) (over 1000kb) | | | | | P |
| 5927 | female | 17 m | CHD,developmental delay | del(7)(q11.23) (over 1000kb) | | | | | P |
| 12367 | female | 9y | facial dysmorphism,intellectual disability | del(7)(q11.23)[hg19,(chr7:73,442,119-74,175,022)]  (over 700kb) | | | | | P |
| 13693 | male | 10y | SGA,intellectual disability | del(7)(q11.23)[hg19,(chr7:73,442,119-74,175,022)]  (over 700kb) | | | | | P |
| 9578 | female | 10y5 m | facial dysmorphism,CHD | del(7)(q11.23)[hg19,(chr7:73,442,119-74,175,022)]  (over 700kb) | | | | | P |
| 12497 | male | 1 m | facial dysmorphism,CHD | del(7)(q11.23)[hg19,(chr7:73,442,119-74,175,022)]  (over 700kb) | | | | | P |
| 12480 | male | 5y | facial dysmorphism,cryptorchidism | del(18)(p11.31-p11.21)[hg19,(chr18:2,916,992-  12,884,236)] (over10000kb) | | | | | P |
| 10850 | female | 7y | facial dysmorphism,intellectual disability,CHD,SGA | del(18)(p11.31-p11.21)[hg19,(chr18:2,916,992-  12,884,236)] (over 9900kb) | | | | | P |
| 8339 | female | 11 m | facial dysmorphism,developmental delay | del(18)(p11.31-p11.21)[hg19,(chr18:2,916,992-  12,377,275)](over 9400kb) | | | | | P |
| 8526 | male | 3y | facial dysmorphism,cryptorchidism | del(17)(p13.3) [hg19,(chr17:1,247,834-1,680,868)]  (over 400kb) | | | | | LP |
| 8551 | female | 6y | facial dysmorphism,CHD | del(17)(p13.3)[hg19,(chr17:1,247,834-1,680,868)]  (over 400kb) | | | | | LP |
| 14170 | female | 7y | facial dysmorphism | del(17)(p13.3)[hg19,(chr17:411,908-1,948,259)]  (over 1500kb) | | | | | LP |
| 13048 | male | 5y | small penis,developmental delay | del(17)(p11.2)[hg19,(chr17:17,115,527-19,580,909)]  (over 2400kb) | | | | | P |
| 3930 | male | 8y | cryptorchidism,developmental delay | del(17)(p12-p11.2)[hg19(chr17:15,801,183-20,274,157)](4473kb) | | | | | P |
| 3660 | male | 2y | cryptorchidism,developmental delay | del(1)(q24.3-q25.3)[hg19(chr1:171,130,803-  185,746,128)(14615kb) | | | | | P |
| 6284 | male | 9y | intellectual disability | del(1)(q24.2-q25.1)[hg19,(chr1:170,501,263-  173,886,516)] (over 3300kb) | | | | | P |
| 6409 | female | 21 m | developmental delay | del(1)(q24.2-q25.1)[hg19,(chr1:168,250,278-  173,886,516)](over 5000kb) | | | | | P |
| 12612 | male | 4y | facial dysmorphism,developmental delay | del(4)(p16.3)[hg19,(chr1:168,250,278-173,886,516)](over 5000kb);dup(21)(q22.3)[hg19,(chr21:46,305,869-  47,865,682)](over 1500kb） | | | | | P |
| 7765 | male | 3y | developmental delay | del(1)(p36.33-p36.31)[hg19,(chr1:1,950,768-6,551,761)]  (over 4500kb) | | | | | P |
| 9726 | female | 5y | developmental delay | dup(1)(q42.2-q44)[hg19,(chr1:230,838,270-  247,612,406)](over 16000kb） | | | | | P |
| 7951 | female | 9 m | facial dysmorphism,developmental delay,CHD,spina bifida, laryngomalacia | del(1)(p36.33-p36.23)[hg19,(chr1:955,503-  7,829,766)](over 6800kb) | | | | | P |
| 12665 | male | 12y | facial dysmorphism,skeletal dysplasia,intellectual disability,ear deformity | dup(1)(q42.13-q44)[hg19,(chr1:229,566,993-247,612,406)](over 18000kb);del(15)(q26.3)[hg19,(chr15:99,19  1,768-101,792,253)](over 1600kb) | | | | | P |
| 4041 | male | 2y | facial dysmorphism,CHD,cleft lip and palate | del(2)(q32.3-q33.2)[hg19(chr2:193,730,505-  204,701,813)](10971kb) | | | | | P |
| 4557 | female | 4 m | facial dysmorphism,developmental delay,CHD,microcephaly | del(2)(q24.2-q31.1)[hg19(chr2:(157205510-  170457666)](13252kb) | | | | | P |
| 6378 | female | 6 m | CHD,hearing abnormalities,vision abnormalities | dup(2)(p25.3)[hg19,(chr2:1,417,233-3,750,260)](over 2300kb);  del(11)(q24.1-q25)[hg19,(chr11:122,942,714-  134,135,746)](over 1200kb) | | | | | P |
| 8905 | female | 9y | facial dysmorphism,skeletal dysplasia,intellectual disability,ear deformity | del(2)(q37.3)[hg19,(chr2:239,152,679-242,708,231)]  (over 3500kb) | | | | | P |
| 8884 | male | 2 m | developmental delay | dup(2)(p24.1-16.3)[hg19,(chr2:20,110,029-  51,259,674)](over 31000kb) | | | | | P |
| 9400 | female | 8y | facial dysmorphism,  intellectual disability,microcephaly | del(2)(q37.3)[hg19,(chr2:239,969,864-242,708,231)](over 2700kb);dup(9)(q34.3)[hg19,(chr9:140,149,752-  140,730,578)](over 500kb) | | | | | P |
| 6803 | female | 7y | skeletal dysplasia,deafness | dup(2)(p11.2-p13.2)[hg19,(chr2:71,693,832-86,565,206)]  (over 15000kb) | | | | | P |
| 11516 | male | 7y | intellectual disability | del(2)(p21-p16.3)[hg19,(chr2:47,596,287-  49,381,666)](over 1800kb) | | | | | P |
| 7033 | female | 8y | intellectual disability | del(5)(p15.33)[hg19,(chr5:218,338-1,816,167)](over  1600kb); | | | | | P |
| 8284 | male | 2y | developmental delay,cryptorchidism | del(5)(p15.33-p15.1)[hg19,(chr5:218,338-  16,617,094)](over 16000kb); | | | | | P |
| 8142 | female | 6y | facial dysmorphism,intellectual disability | dup(6)(p25.3-p22.3)[hg19,(chr6:391,739-  18,155,400)](over 17000kb) | | | | | P |
| 7685 | female | 18y | intellectual disability | del(6)(q22.1)[hg19,(chr6:116,440,085-117,923,705)]  (over 1400kb) | | | | | P |
| 6640 | male | 4y | facial dysmorphism | del(6)(p21.1)[hg19,(chr6:41,126,244-43,021,683)](over  1900kb） | | | | | P |
| 11167 | female | 7y | short stature | del(6)(q25.1-q25.2)[hg19,(chr6:149,539,060-  152,958,497)](over 3400kb); | | | | | P |
| 10239 | male | 2y | facial dysmorphism,intellectual disability | del(7)(q33-q35)[hg19,(chr7:137,761,205-  144,533,146)](over 6700kb); | | | | | P |
| 6897 | female | 16y | intellectual disability | del(7)(q33-q34)[hg19,(chr7:137,761,178-  140,624,728)](over 2900kb); | | | | | P |
| 12721 | male | 1y6 m | facial dysmorphism,developmental delay,SGA | del(7)(q36.1-q36.3)[hg19,(chr7:150,642,044-157,210,133)](over 6500kb);dup(18)(q23)[hg19,(chr18:77,439,801-  77,514,510)](over 200kb) | | | | | P |
| 12260 | female | 6y | facial dysmorphism,skeletal dysplasia | del(8)(q23.3-q24.11)[hg19,(chr8:116,420,724-119,124,058)](over 2700kb); | | | | | P |
| 8164 | female | 1y | developmental delay | del(9)(q33.3-q34.11)[hg19,(chr9:129,376,722-  131,395,944)](over 2000kb); | | | | | P |
| 8720 | female | 3y | facial dysmorphism,developmental delay | del(9)(q31.2-q31.3)[hg19,(chr9:108,320,411-  113,563,278)](over 5200kb); | | | | | P |
| 2882 | female | 6y | facial dysmorphism,intellectual disability,SGA,CHD | del(9)(q21.11-q21.31)[hg19,(chr9:71000154-  83236029)](12236kb); | | | | | P |
| 9057 | male | 8y | intellectual disability,microcephaly | del(10)(q26.13-26.2)[hg19,(chr10:124,221,041-127,511,837)] (over 3200kb) | | | | | P |
| 10424 | male | 5y | developmental delay | del(12)(q24.31)[hg19,(chr12:122,755,981-  124,246,301)](over 1400kb） | | | | | P |
| 13003 | female | 2y | developmental delay | del(12)(p13.33-p13.31)[hg19,(chr12:389,223-  6,484,729)](over 6000kb) | | | | | P |
| 7767 | female | 6y | intellectual disability,SGA,CHD | del(13)(q31.1-q32.1)[hg19,(79,314,118-  96,544,277)](17230kb) | | | | | P |
| 8046 | male | 11y | intellectual disability,anal fistula | del(13)(q34)(over 3000kb) | | | | | P |
| 3626 | male | 2m | developmental delay | del(15)(q11.2-q13.1)[hg19(23,707,494-  28,525,454)](4818kb) | | | | | P |
| 7177 | female | 7y | SGA | del(15)(q26.3)[hg19,(chr15:99,191,768-101,792,137)]  (over 2600kb) | | | | | P |
| 8120 | female | 7y1 m | intellectual disability | dup(16)(p13.11)[hg19,(chr16:15,737,124-16,317,328)](over 500kb) | | | | | LP |
| 9951 | female | 1y6 m | facial dysmorphism,intellectual disability,SGA | del(16)p13.11[hg19,(chr16:15,737,124-16,317,328)(over 500kb) | | | | | LP |
| 5766 | female | 11y | short stature | dup(16)(p11.2)(over 300kb) | | | | | P |
| 5548 | male | 3y | facial dysmorphism,developmental delay | dup(17)(p11.2)(over 3000kb) | | | | | P |
| 13727 | female | 7y | intellectual disability,SGA | dup(19)(p13.3)[hg19,(chr19:852,303-6,720,661)](over  5800kb) | | | | | P |
| 5909 | female | 11y | intellectual disability | del(20)(p13)[hg19,(chr20:939,096-2,413,399)](over  1400kb) | | | | | LP |
| 6338 | male | 4y | facial dysmorphism,small penis | del(22)(q13.2)[hg19,(chr22:41,488,614-41,924,993)]  (over 400kb) | | | | | P |
| 9055 | male | 6y | cryptorchidism | del(22)(q12.3-q13.1)[hg19,(chr22:36,649,117-38,380,539)](over 1700kb) | | | | | LP |
| 3977 | female | 13y | intellectual disability,gonadal dysplasia | dup(22)(q11.23)[(hg19)chr22: 23,648,768-  24,995,964](1347kb） | | | | | LP |
| 13661 | male | 12y | intellectual disability | dup(22)(q11.23)[hg19,(chr22:23,915,313-  24,924,358)](over 1000kb） | | | | | P |
| 10822 | male | 3y | developmental delay | duplication of ARID1B | | | | | LP |
| 13508 | male | 4 m | facial dysmorphism,skeletal dysplasia | dup(X)(q26.3-q28)[hg19,(chrX:135,067,586-149,841,616)] (over 14800kb) | | | | | P |
| 4187 | female | 7y9 m | short stature | del(X)(p22.33-p22.32)[(hg19chrX:60,701-4,664,247)]  (over 4600kb)(include *SHOX gene*) | | | | | P |
| 4057 | female | 4y | skeletal dysplasia | del(X)(p22.33-p22.31)[(hg19chrX:60,701-6445238)] (6385kb)(include SHOX gene) | | | | | P |
| 13816 | female | 6y | short stature | large deletion of Xp, large duplication of Xq | | | | | P |
| 10848 | female | 16y | gonadal dysplasia | large deletion of Xp, large duplication of Xq | | | | | P |
| 6036 | male | 7y | small penis, small testicles | 45X/46XY mosaicisms | | | | | P |
| 12368 | male | 12y | small penis, small testicles | 45X/46XY mosaicisms | | | | | P |
| 13120 | male | 5y | cryptorchidism | 47XXY | | | | | P |
| 10618 | female | 17y | gonadal dysplasia | 45X | | | | | P |
| 13796 | female | 12y | facial dysmorphism,CHD | 45X | | | | | P |
| 4037 | female | 7y | gonadal dysplasia,CHD | 45X | | | | | P |
| 8220 | female | 5y | facial dysmorphism | 45X | | | | | P |
| 9210 | female | 7y | facial dysmorphism | 45X | | | | | P |
| 9598 | female | 2y | gonadal dysplasia | 45X | | | | | P |