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## Supplemental Data

# De Novo Mutations of *RERE* Cause a Genetic Syndrome with Features that Overlap Those Associated with Proximal 1p36 Deletions

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## Case Reports

### Subject 1

Subject 1 is a 3-year-old Northern European male who carries a *de novo* c.3466G>A, p.Gly1156Arg missense change in *RERE*. Prenatal ultrasound examinations revealed intrauterine growth retardation. He was born at 35 weeks gestation with a birth weight of 1.64 kg (<3$^{rd}$ centile). Multiple regions of infarction were found in the placenta. His postnatal evaluation revealed bilateral optic colobomas, optic nerve hypoplasia, unilateral microphthalmia, anisometropia, mild sensorineural hearing loss, micrognathia, hypospadias with penile chordee and gastroesophageal reflux disease (GERD). An echocardiogram revealed a ventricular septal defect (VSD) and a patent foramen ovale (PFO). Over time he was also noted to have global developmental delay and mild spastic quadriparesis. He also has dysarthric speech with difficulty in guttural and palatal sound production and swallowing difficulties possibly attributable to cranial nerve dysfunction. A brain MRI obtained at 7 months of age revealed a thin corpus callosum, a small anterior vermis, a small pons with a ventral cleft at the ponto-medullary junction, delayed myelination, and severely decreased white matter volume (Figure 1). At 3 years of age he weighed 16.2 kg (86$^{th}$ centile), his height was 105.3 cm (99$^{th}$ centile) and he had an occipital frontal circumference (OFC) of 50 cm (58$^{th}$ centile).

### Subject 2

Subject 2 is a 15-month-old Northern European male who carries a *de novo* c.4313_4318dupTCCACC, p.1438Leu_1439Hisdup change in *RERE*. He was born at 30 and 6/7 weeks gestation via C-section for symmetric intrauterine growth retardation and fetal distress. His birth weight was 0.94 kg (~3$^{rd}$ centile). Postnatally he was noted to have simple ears, a right-sided, unilateral iris coloboma, choanal atresia, a right-sided multicystic kidney with several right upper pole renal cysts and a large dominant cyst measuring 6 mm, cryptorchidism, and 5th finger clinodactyly with nail hypoplasia. An echocardiogram revealed a VSD, a patent ductus arteriosus (PDA) that was surgically closed, and

anomalous pulmonary venous return (APVR). Diaphragm dysfunction resulted in tracheostomy and ventilator dependence. He was later noted to have developmental delay. A brain MRI obtained at 4 months revealed a thin corpus callosum, ventriculomegaly, incompletely folded hippocampi, and severely diminished white matter volume. At 15 months of age he weighed 8.55 kg (~5$^{th}$ centile), his height was 64 cm (<1$^{st}$ centile), and his OFC was 42.5 cm (<1$^{st}$ centile).

**Subject 3**

Subject 3 is a 2-year-old Hispanic male who carries a *de novo* c.3785C>G, p.Pro1262Arg missense change in *RERE*. At 26 weeks gestation, an ultrasound examination revealed polyhydramnios in the setting of duodenal atresia, a fenestrated choroid plexus, a liver mass, small kidneys and syndactyly. He was born at 37 weeks gestation and weighed 2.92 kg (16$^{th}$ centile). He was noted to have a palpable third fontanelle, hypotelorism, microphthalmia, small and upslanting palpebral fissures, epicanthal folds, abnormal ears with bilateral prominence of the antihelix stem and horizontal crus helix with expanded terminal portion, anterior earlobe creases, bilateral preauricular pits, micrognathia, small nipples, and a sacral hair tuft. He also has bilateral, almost complete, syndactyly of the third and 4th fingers, unilateral partial syndactyly between the first and second fingers, long thumbs and 5th toes and atypical creases of the palm secondary to syndactyly. An ophthalmological evaluation revealed Peter's anomaly of the right eye, a stable, inferonasal opacity, and bilateral iris abnormalities. Ultrasound examinations revealed a VSD that resolved by age 1, bilateral hydronephrosis with grade 2-4 vesicoureteral reflux which is resolving spontaneously, and an annular pancreas. He was later noted to have developmental delay and hypotonia. He is being treated with levetiracetam due to a history of staring spells and an EEG examination that showed cortical irritability. An MRI obtained at 1 year and 6 months showed a thin corpus callosum, deep primary fissure of the cerebellar vermis, ventriculomegaly, and severely diminished white matter volume. At 2 years and 4 months of age his weight was 10.34 kg (1$^{st}$ centile), his length was 82 cm (2$^{nd}$ centile), and his OFC was 46.4 cm (4$^{th}$ centile).

**Subject 4**

Subject 4 is a 9-year-old Northern European female with a *de novo* c.4293C>G, p.His1431Gln missense change in *RERE*. She was also found to be mosaic for a *de novo* c.2464G>A, p.Gly822Ser change in the sodium channel, voltage gated, type II alpha subunit gene (*SCN2A* [OMIM: 182390]). This *SCN2A* change is predicted to be probably damaging by PolyPhen-2, damaging by SIFT and disease causing by MutationTaster. Mutations in *SCN2A* have been implicated in two autosomal dominant disorders: epileptic encephalopathy, early infantile, 11 [OMIM: 613721] and seizures, benign familial infantile, 3 [OMIM: 607745].

Pregnancy was complicated by a motor vehicle accident at 10 weeks with a normal follow-up ultrasound evaluation. She was born at 39 weeks and had some transient hypoglycemia and temperature instability. She was noted to have deep-set eyes, epicanthal folds, fleshy auricles, a deep furrow in the posterior 1/3 of the tongue, bilateral single palmar creases, broad thumbs and mild brachydactyly. In the neonatal period she was found to have developmental hip dysplasia and severe vesicoureteral reflux requiring surgery. She is hypotonic and has moderate intellectual disability, severe behavioral issues and seizures. An MRI obtained at 1 year and 2 months showed a thin corpus callosum, a diminished cerebellar vermis with deep fissures, and significantly diminished white matter volume. At 9 years and 7 months of age her weight was 39 kg (89$^{th}$ centile), her height was 137 cm (57$^{th}$ centile), and her OFC was 54 cm (60$^{th}$ centile).

**Subject 5**

Subject 5 is a 12-year 8-month-old Dutch male (reported previously by Bosch et al. as Patient 22) with a *de novo* c.4293C>A change in *RERE* that results in the same amino acid change as Subject 4 (p.His1431Gln).[22] He was born at 40 weeks gestation and weighed 4.19 kg (~95$^{th}$ centile). He has frontal bossing, fleshy auricles with squared superior portions, deep-set eyes, bilateral blepharophimosis, a bulbous nose, full lips, broad, large incisors, broad alveolar ridges, and a small, high arched palate. Eye and vision problems include strabismus, bilateral optic atrophy and cerebral visual impairment. He has a

history of recurrent upper airway infections, vesicoureteral reflux, feeding problems with GERD and pyloric hypertrophy which required surgical intervention. He has significant developmental delay. An evaluation performed at 9 years 1 month of age revealed gross motor achievement of a 24-month-old, fine motor abilities of a 9 to12-month-old, the receptive language of a 6 to 9-month-old and the social skills of a 12-month-old. At 8 years of age he developed epilepsy. He takes carbamazepine but still has several complex partial seizures a day. His MRI at 3 years and 6 months of age showed an abnormal corpus callosum with blunting of the rostrum, mild to moderate ventriculomegaly, a small cerebellar vermis, and globally diminished white matter volume. At ten years of age his height was 157 cm (>99$^{th}$ centile), and his OFC was 55.5 cm (~95$^{th}$ centile).

**Subject 6**

Subject 6 is a 6-year-old adopted Northern European/Hispanic female with a c.3122delC, p.Pro1041Lysfs*40 frameshift change in *RERE*. Parental DNA is not available. Since this change occurs in the 17$^{th}$ of 21 *RERE* coding exons [NM_012102], it may trigger nonsense-mediated mRNA decay. Pregnancy and birth history are limited, but there was reported alcohol use during the pregnancy. She was born near term and had no perinatal complications. Her family history is positive for intellectual disability and mental illness in her biological mother, and intellectual disability in both of her maternal grandparents and a maternal half-uncle. Her dysmorphic features include macrocephaly, a triangular-shaped face, hypertelorism, broad, sparse eyebrows, low set and posteriorly rotated ears, anteverted nares, and a mildly flattened philtrum. She has hypotonia, myopia, lumbar lordosis, and small hands with broad thumbs. Developmental milestones were delayed, with walking and first words both around 2 years of age. She is now enrolled in a special education program. She has problems with coordination, behavioral tantrums, and she engages in self-injurious behavior including head banging and nail biting. At 6 years of age her height was 108 cm (6$^{th}$ percentile), her weight was 21.7 kg (63$^{rd}$ percentile) and her OFC was 54.1 cm (>98$^{th}$ percentile).

**Subject 7**

Subject 7 is an 11-year-old Dutch male who carries a *de novo* c.1411G>A, p.Val471Ile missense change in *RERE*. He was born at 34 weeks gestation with a weight of 2.24 kg (~5th centile). This twin pregnancy was complicated by maternal hypertension for which mother used medication. He has an older sister who is healthy but his twin sister was recently diagnosed with KBG syndrome. Parents are non-consanguineous. After birth, he was noted to be hypotonic and to have a cleft lip, down slanting palpebral fissures and a unilateral single palmar crease. He required tube feeding during the first three weeks of life. His cleft lip was surgically repaired at three years of age. He has a history of developmental delay, was diagnosed with ADHD, and has mild intellectual disabilities for which he attends a special needs school. An MRI obtained at 7 years 9 months of age showed an abnormal corpus callosum with blunting of the rostrum, a small anterior commissure, and diminished white matter volume. Cardiac and renal ultrasound did not reveal any abnormalities. At 11 years 6 months of age his height was 127 cm (<0.1 centile), his weight was 24 kg ($2^{nd}$ centile), and his OFC was 49.9 cm ($0.5^{th}$ centile).

**Subject 8**

Subject 8 is a 10-year-old Northern European male who carries a c.1104delA, p.Leu369Cysfs*15 change in *RERE*. This variant was not present in his mother but a paternal DNA sample could not be obtained for testing. Since this change occurs in the last nucleotide of the $9^{th}$ of 21 *RERE* coding exons [NM_012102], it may trigger nonsense-mediated mRNA decay. Pregnancy was complicated by anemia, vaginal infection, and maternal smoking and alcohol consumption until the pregnancy was recognized. He was born at 36 weeks gestation by Cesarean section for failure to progress. At birth, his weight was 3.3 kg (~$35^{th}$ centile), he was 46 cm in length ($35^{th}$ centile) and his OFC was 38 cm (>$98^{th}$ centile). After birth he had feeding difficulties with a poor latch and suck, sleeping difficulties, gastroesophageal reflux with colic, food allergies, and chronic ear infections. He has an astigmatism in his right eye and wears glasses. Dysmorphic features include a widows peak, mild down-slanting palpebral fissures, increased eyebrow hair laterally, narrow dental arches, small lower arch teeth, micrognathia, inverted nipples, small hands

(~5th centile palm and finger lengths) and 5th finger clinodactyly. His gross motor development was normal with walking at 11 months, but he had fine motor and speech delay and was later diagnosed with autism spectrum disorder and ADHD. A brain MRI ordered for developmental delay was normal. At the age of 10 years and 4 months his weight was 28.1 kg (16th centile), his height was 131 cm (10th centile) and his OFC was 55.5 cm (90th centile).

**Subject 9**

Subject 9 is a 7-year old male who has a *de novo* c.2249_2270dup p.Thr758Serfs*36 mutation. He was born via induced vaginal delivery after an uncomplicated pregnancy at 42 and 2/7 weeks gestation with a weight of 4.50 kg (98th centile). In the neonatal period he demonstrated poor suck and swallow, making breastfeeding difficult. He had severe speech and language delay and was diagnosed with intellectual disability and autism. He has a ventricular septal defect (VSD). His dysmorphic features include macrocephaly—possibly familial since his mother's OFC is 59.7 cm (+ 2.5 SD)—frontal bossing and scoliosis. He has a small mouth and five café au lait patches, both of which are seen in his father. He has a younger sister with autism, a paternal uncle who died of Duchenne muscular dystrophy and a paternal uncle who died of acute heart failure at 20 years of age. An MRI at 6 years 10 months of age showed mildly diminished white matter volume and a small splenium of the corpus callosum. At 6 years 10 months of age his height was 131 cm (94th centile), his weight was 26 kg (82nd centile) and his OFC was 57.3 cm (>99th centile).

**Subject 10**

While investigating the genetic causes of autism spectrum disorder in a large cohort, Krumm et al. identified a 14-year-old Non-Hispanic female with an autism spectrum disorder who carried a *de novo* c.2278C>T, p.Gln760* change in *RERE* (subject 11654.p1).[23] We refer to her here as Subject 10. She was born at 40 weeks via cesarean section due to failure to progress. At birth she weighed 4.03 kg (95th centile), was 53.3 cm in length (99th centile) and her OFC was noted to be larger than average but no

measurements were recorded. She has sleep difficulties—sleep apnea, and breathing difficulties—as well as incontinence at night. She was diagnosed with an autism spectrum disorder using the ADOS and ADI-R. On the DAS-II, her cognitive, verbal, and non-verbal abilities were measured to be in the very low range (General Conceptual Ability = 40). On the Social Responsiveness Scale, she obtained a t-score of 89, which is in the severe range. On the Vineland II she achieved an Adaptive Behavior Composite score of 70, which indicates that her adaptive behavior skills were moderately low.

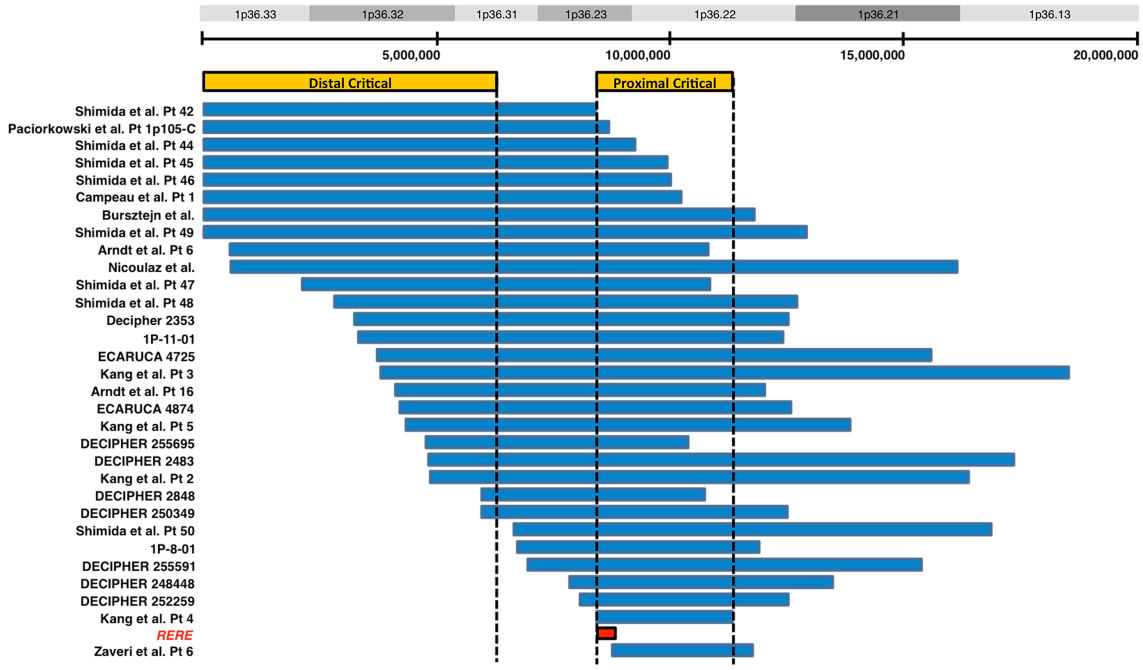


**Figure S1: Published and unpublished terminal and interstitial deletions of chromosome 1p36 that include *RERE*.**

The first 20 Mb of chromosome 1p36 are represented along with the approximate locations of the distal and proximal 1p36 critical regions (orange bars) and the *RERE* gene (red bar). The location of deletions identified in individual patients are shown (blue bars) with their associated reference. Individuals 1P-11-01 and 1P-08-01 have not been published previously. These individuals were accrued into an IRB approved study at Baylor College of Medicine after informed consent was obtained.

Table S1. Phenotypic descriptions of Subjects 1-10.

| | S1 | S2 | S3 | S4 | S5 | S6 | S7 | S8 | S9 | S10 | Total | Described In 1p36 Deletion Cohort? |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age** | 3yr | 15 m | 2yr | 9yr | 12yr | 6yr | 11yr | 10yr | 7yr | 14yr | | |
| **Sex** | M | M | M | F | M | F | M | M | M | F | | |
| **Neurologic** | | | | | | | | | | | **10/10 (100%)** | |
| ID/DD/Autism | + | + | + | + | + | + | + | + | + | + | 10/10 (100%) | Yes |
| Seizures | - | - | -[a] | +[b] | + | - | - | - | - | - | 2/10 (20%) | Yes |
| Hypotonia | - | - | + | + | - | + | + | - | - | - | 4/10 (40%) | Yes |
| Behavioral problems | - | - | - | + | - | + | - | - | - | - | 2/10 (20%) | Yes |
| Spastic quadriparesis | + | - | - | - | - | - | - | - | - | - | 1/10 (10%) | No |
| ADHD | - | - | - | - | - | - | + | + | - | - | 2/10 (20%) | No[c] |
| Feeding/swallowing problems | + | - | - | - | + | - | + | + | + | - | 5/10 (50%) | Yes |
| **CNS anomalies** | | | | | | | | | | | **7/8 (88%)** | |
| Abnormal, thin corpus callosum | + | + | + | + | + | N/A | + | - | - | N/A | 6/8 (75%) | Yes |
| Diminished white matter volume | + | + | + | + | + | N/A | + | - | - | N/A | 6/8 (75%) | No |
| Abnormal cerebellar vermis | + | - | + | + | + | N/A | - | - | - | N/A | 4/8 (50%) | No |
| Ventriculomegaly | - | + | + | - | + | N/A | - | - | - | N/A | 3/8 (38%) | Yes |
| Small pons | + | - | - | - | - | N/A | - | - | - | N/A | 1/8 (13%) | No |
| Abnormal hippocampus | - | + | - | - | - | N/A | - | - | - | N/A | 1/8 (13%) | No |
| Small anterior commissure | - | - | - | - | - | N/A | + | - | - | N/A | 1/8 (13%) | No |
| Delayed myelination | + | - | - | - | - | N/A | - | - | + | N/A | 2/8 (25%) | Yes |
| **Ophthalmologic** | | | | | | | | | | | **4/10 (40%)** | |
| Coloboma | + | + | - | - | - | - | - | - | - | - | 2/10 (20%) | Yes |
| Optic nerve atrophy/hypoplasia | + | - | - | - | + | - | - | - | - | - | 2/10 (20%) | No[d] |
| Microphthalmia | + | - | + | - | - | - | - | - | - | - | 2/10 (20%) | Yes |
| Peter's anomaly | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) | No |
| Iris anomalies | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) | Yes |
| Blepharophimosis | - | - | - | - | + | - | - | - | - | - | 1/10 (10%) | No |
| **Auditory** | | | | | | | | | | | **1/10 (10%)** | |
| Sensorineural hearing loss | + | - | - | - | - | - | - | - | - | - | 1/10 (10%) | Yes |
| **Craniofacial** | | | | | | | | | | | **2/10 (20%)** | |
| Choanal atresia | - | + | - | - | - | - | - | - | - | - | 1/10 (10%) | No[e] |
| Cleft Lip | - | - | - | - | - | - | + | - | - | - | 1/10 (10%) | Yes |
| **Cardiac** | | | | | | | | | | | **4/10 (40%)** | |
| VSD | + | + | + | - | - | - | - | - | + | - | 4/10 40%) | Yes |
| PFO | + | - | - | - | - | - | - | - | - | - | 1/10 (10%) | No[f] |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PDA | - | + | - | - | - | - | - | - | - | - | 1/10 (10%) | Yes |
| APVR | - | + | - | - | - | - | - | - | - | - | 1/10 (10%) | Yes |
| **Gastrointestinal** | | | | | | | | | | | **4/10 (40%)** | |
| GERD | + | - | - | + | + | - | - | + | - | - | 3/10 (30%) | Yes |
| Duodenal atresia | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) | Yes |
| Annular pancreas | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) | No |
| Pyloric hypertrophy | - | - | - | - | + | - | - | - | - | - | 1/10 (10%) | No |
| **Genitourinary** | | | | | | | | | | | **5/10 (50%)** | |
| Vesicoureteral reflux | - | - | + | + | + | - | - | - | - | - | 3/10 (30%) | No |
| Cystic kidney | - | + | - | - | - | - | - | - | - | - | 1/10 (10%) | No |
| Hypospadias | + | - | - | N/A | - | N/A | - | - | - | N/A | 1/7 (14%) | No |
| Cryptorchidism | - | + | - | N/A | - | N/A | - | - | - | N/A | 1/7 (14%) | Yes |
| **Musculoskeletal** | | | | | | | | | | | **4/10 (40%)** | |
| Syndactyly | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) | No |
| Hip dysplasia | - | - | - | + | - | - | - | - | - | - | 1/10 (10%) | Yes |
| Scoliosis | - | - | - | - | - | - | - | - | + | - | 2/10 (20%) | Yes |
| Lumbar lordosis | - | - | - | - | - | + | - | - | - | - | 1/10 (10%) | No |
| **Growth** | | | | | | | | | - | | **7/10 (70%)** | |
| IUGR | + | + | - | - | - | - | - | - | - | - | 2/10 (20%) | No |
| Tall stature ($\geq 98^{th}$ centile) | + | - | - | - | + | - | - | - | - | N/A | 2/9 (22%) | No |
| Short stature ($\leq 2^{nd}$ centile) | - | + | + | - | - | - | + | - | - | N/A | 3/9 (33%) | Yes |
| Macrocephaly ($\geq 98^{th}$ centile) | - | - | - | - | - | + | - | - | + | N/A | 2/9 (22%) | No |
| Microcephaly ($\leq 2^{nd}$ centile) | - | + | - | - | - | - | + | - | - | N/A | 2/9 (22%) | Yes |

+ = feature was documented in this subject, - = feature was not documented in this patient , N/A = not applicable or required study/data not obtained, a = staring spells, b = subject is mosaic for a putatively deleterious *de novo* change in *SCNA2*, a gene known to cause autosomal dominantly inherited seizures. c = one individual was noted to have hyperactivity, d = several individuals with 1p36 deletions were reported to have nystagmus which may be a symptom of optic atrophy, e = one individual was described as having nasal cavity stenosis, f = secundum ASDs are reported. ADHD = Attention deficit hyperactivity disorder, APVR = anomalous pulmonary venous return, DD = developmental dealay, GERD = gastroesophageal reflux disease, ID = intellectual disability, IUGR = intrauterine growth retardation, PDA = patent ductus arteriosus, PFO = patent foramen ovale, VSD = ventricular septal defect.

Table S2. Dysmorphic features observed in Subjects 1-10.

| | S1 | S2 | S3 | S4 | S5 | S6 | S7 | S8 | S9 | S10 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Head** | | | | | | | | | | | |
| Third fontanel | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| Frontal bossing | - | - | - | - | + | - | - | - | + | - | 2/10 (20%) |
| Triangular face | - | - | - | - | - | + | - | - | - | - | 1/10 (10%) |
| **Eyes** | | | | | | | | | | | |
| Abnormal eyebrows | - | - | - | - | - | + | - | + | - | - | 2/10 (20%) |
| Hypotelorism | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| Hypertelorism | - | - | - | - | - | + | - | - | - | - | 1/10 (10%) |
| Upslanting palpebral fissures | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| Down-slanting palpebral fissures | - | - | - | - | - | - | + | + | - | - | 2/10 (20%) |
| Small palpebral fissures | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| Epicanthal folds | - | - | + | + | - | - | - | - | - | - | 2/10 (20%) |
| Deeply set eyes | - | - | - | + | + | - | - | - | - | - | 2/10 (20%) |
| Blepharaophymosis | - | - | - | - | + | - | - | - | - | - | 1/10 (10%) |
| **Ears** | | | | | | | | | | | |
| Abnormal ears | - | + | + | + | + | + | - | - | - | - | 5/10 (50%) |
| Preauricular pits | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| **Nose** | | | | | | | | | | | |
| Bulbous nose | - | - | - | - | + | - | - | - | - | - | 1/10 (10%) |
| Anteverted nares | - | - | - | - | - | + | - | - | - | - | 1/10 (10%) |
| **Philtrum/lips** | | | | | | | | | | | |
| Flat philtrum | - | - | - | - | - | + | - | - | - | - | 1/10 (10%) |
| Full lips | - | - | - | - | + | - | - | - | - | - | 1/10 (10%) |
| **Oral cavity/Jaw** | | | | | | | | | | | |
| Small mouth | - | - | - | - | - | - | - | - | + | - | 1/10 (10%) |
| Furrowed tongue | - | - | - | + | - | - | - | - | - | - | 1/10 (10%) |
| Abnormal teeth | - | - | - | - | + | - | - | + | - | - | 2/10 (20%) |
| Broad alveolar ridges | - | - | - | - | + | - | - | - | - | - | 1/10 (10%) |
| High arched palate | - | - | - | - | + | - | - | - | - | - | 1/10 (10%) |
| Micrognathia | + | - | + | - | - | - | - | + | - | - | 3/10 (30%) |
| **Chest** | | | | | | | | | | | |
| Small nipples | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| Inverted nipples | - | - | - | - | - | - | - | + | - | - | 1/10 (10%) |
| **Extremities** | | | | | | | | | | | |
| Small hands | - | - | - | - | - | + | - | + | - | - | 2/10 (20%) |
| Syndactyly | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| 5$^{th}$ Finger Clinodactyly | - | + | - | - | - | - | - | + | - | - | 2/10 (20%) |
| Digital anomalies | - | - | + | + | - | + | - | - | - | - | 3/10 (30%) |
| Nail hypoplasia | - | + | - | - | - | - | - | - | - | - | 1/10 (10%) |
| Abnormal palmar creases | - | - | + | + | - | - | + | - | - | - | 3/10 (30%) |
| **Hair/Skin** | | | | | | | | | | | |
| Widow's Peak | - | - | - | - | - | - | - | + | - | - | 1/10 (10%) |
| Sacral hair tuft | - | - | + | - | - | - | - | - | - | - | 1/10 (10%) |
| Café Au Lait spots | - | - | - | - | - | - | - | - | + | - | 1/10 (10%) |