

Table S1 The genotype/phenotype(s) of 60 21q22.3 deletion cases that overlapped with present patient in DECIPHER

DECIPHER Patient	Sex	Location (GRCh38/hg38)	Size	Inheritance/genotype	Pathogenicity/contribution	Phenotype(s)
396146	46XX	21:30205811-46699983	16.49 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Abnormal dermatoglyphics, broad palm, bulbous nose, cubitus valgus, decreased fetal movement, dental malocclusion, downturned corners of mouth, EEG abnormality, elbow flexion contracture, hip dislocation, hypoplastic philtrum, hypotonia, incoordination, intellectual disability, keratoconus, long eyelashes, low anterior hairline, malar flattening, mandibular prognathia, myopia, nasal speech, obesity, pes planus, premature birth, round face, short metacarpal, short neck, short philtrum, spotty hyperpigmentation, synophrys, tapered finger, thin lower lip vermilion, thin upper lip vermilion, upslanted palpebral fissure
395927	46XX	21:30205811-46699983	16.49 Mb	De novo	Likely pathogenic	Abnormal aortic morphology, abnormality of prenatal development or birth, aortic valve stenosis, arrhythmia, atrial septal defect, camptodactyly of finger, cleft of alveolar ridge of maxilla, coarctation of aorta, convex nasal ridge, ectopic anus, hemivertebrae, hydrocephalus, hypertonia, hypoplasia of the corpus callosum, hypoplastic left heart, micrognathia, microphthalmia, overlapping fingers, patent ductus arteriosus, preauricular skin tag, prominent glabella, prominent nasal bridge, protruding ear, renal dysplasia, renal hypoplasia, sclerocornea, short neck, short stature, supernumerary ribs, wide intermamillary distance
398086	46XX	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Abnormal dermatoglyphics, abnormality of the dentition, abnormally low-pitched voice, blepharitis, brachycephaly, broad palm, brushfield spots, conjunctivitis, depressed nasal bridge, epicanthus, furrowed tongue, high palate, hypothyroidism, hypotonia, intellectual disability, joint laxity, myopia, narrow palate, primary microcephaly, sandal gap, short neck, short stature, single transverse palmar crease, small hand, strabismus, upslanted palpebral fissure, ventricular septal defect
396000	46XX	21:41106204-46699983	5.59 Mb	De novo, mosaic	Likely pathogenic	Abnormal hip joint morphology, abnormal thrombocyte morphology, abnormality of the pinna, breech presentation, delayed speech and language development, downslanted palpebral fissures, EEG abnormality, flexion contracture, high pitched voice, hydrocephalus, hypertonia, intellectual disability, low-set ears, macrotia, micrognathia, non-midline cleft lip, patent ductus arteriosus, primary microcephaly, recurrent infections, short neck, short stature, small for gestational age, strabismus, telecanthus, umbilical hernia, wide nasal bridge
394833	46XX	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Absent toe, breech presentation, cerebral atrophy, convex nasal ridge, cutis marmorata, fine hair, high anterior hairline, high palate, hydrocephalus, hypermobility of toe joints, hypotonia, intellectual disability, joint laxity, low-set ears, microcephaly, micrognathia, narrow forehead, prominent metopic ridge, prominent occiput, scoliosis, short foot, short nose, short toe, small for gestational age, strabismus
393928	46XY	21:38306208-46699983	8.39 Mb	De novo, mosaic	Likely pathogenic	Adducted thumb, broad neck, camptodactyly of finger, cryptorchidism, downslanted palpebral fissures, epicanthus, hypoplastic philtrum, hypotonia, inguinal hernia, intellectual disability, long neck, long philtrum, micrognathia, microtia, narrow chest, narrow forehead, narrow mouth, overlapping fingers, prominent antihelix, prominent nasal bridge, prominent occiput, proportionate short stature, thin upper lip vermilion, wide nasal bridge
398079	46XX	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Abnormal dermatoglyphics, abnormality of the helix, blepharitis, brachycephaly, broad palm, brushfield spots, depressed nasal bridge, diastasis recti, epicanthus, finger clinodactyly, furrowed tongue, high palate, hypermetropia, hypotonia, narrow palate, primary microcephaly, sandal gap, short 5th finger, short neck, short stature, small for gestational age, small hand, upslanted palpebral fissure
393304	46XY	21:30205811-46699983	16.49 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Abnormality of the pinna, abnormality of the skin, adipose tissue loss, downslanted palpebral fissures, epicanthus, facial asymmetry, high palate, hip dislocation, hypertelorism, hypertonia, hypospadias, low-set ears, micropenis, narrow chest, scrotal hypoplasia, short palpebral fissure, short stature, small for gestational age, talipes equinovaglus, torticollis, wide intermamillary distance
395104	46XX	21:30205811-46699983	16.49 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Abnormality of the pinna, coarse hair, finger clinodactyly, full cheeks, genu valgum, hallux valgus, high palate, highly arched eyebrow, hypertelorism, hypoplastic nipples, incoordination, intellectual disability, low-set ears, microdontia, short nose, strabismus, talipes equinovarus, thick eyebrow, thick nasal alae, wide intermamillary distance
395134	46XY	21:30205811-46699983	16.49 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Abnormality of the pinna, broad neck, coarse hair, flat occiput, full cheeks, genu valgum, hallux valgus, high palate, highly arched eyebrow, hypertelorism, incoordination, intellectual disability, microdontia, micropenis, prominent ear helix, round face, strabismus, talipes equinovarus, thick eyebrow, turriccephaly
393029	46XX	21:30205811-46699983	16.49 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Abnormality of the helix, abnormality of the pinna, aortic valve stenosis, bulbous nose, downslanted palpebral fissures, EEG abnormality, epicanthus, facial asymmetry, intellectual disability, long philtrum, micrognathia, malar flattening, nasal speech, non-midline cleft lip, pes planus, prominent nasal bridge, recurrent infections, short 5th finger, thick upper lip vermilion, wide mouth
401735	46XY	21:40288955-45858283	5.57 Mb	De novo	Likely pathogenic	Atopic dermatitis, autistic behavior, cleft mandible, cleft palate, coarse hair, delayed speech and language development, down-sloping shoulders, downslanted palpebral fissures, feeding difficulties in infancy, hypotonia, long philtrum, micrognathia, malar flattening, nasal speech, non-midline cleft lip, pes planus, prominent nasal bridge, recurrent infections, short 5th finger, thick upper lip vermilion
393862	46XX	21:38306208-46699983	8.39 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Anteverted nares, bulbous nose, cleft palate, finger clinodactyly, hammertoe, hypotonia, intellectual disability, micrognathia, non-midline cleft lip, preauricular pit, pulmonic stenosis, recurrent infections, sacral dimple, small for gestational age, trigonocephaly, upslanted palpebral fissure, vesicoureteral reflux
393893	46XY	21:41106204-46699983	5.59 Mb	De novo	Likely pathogenic	Abnormality of the pinna, downslanted palpebral fissures, finger clinodactyly, hypertonia, inguinal hernia, intellectual disability, low-set ears, microcephaly, micrognathia, overlapping toe, plagiocephaly, prominent metopic ridge, small for gestational age, small nail, spotty hyperpigmentation, thick upper lip vermilion, thin ribs
400843	46XX	21:30205812-46699983	16.49 Mb	De novo, mosaic	Likely pathogenic	Abnormal acetabulum morphology, abnormal ilium morphology, abnormal thumb morphology, concave nail, deeply set eye, hypoplastic philtrum, joint laxity, low-set ears, micrognathia, misalignment of teeth, pectus excavatum, pes planus, preauricular pit, preauricular skin tag, slender build, stenosis of the external auditory canal, umbilical hernia
395494	46XX	21:41106204-46699983	5.59 Mb	De novo	Likely pathogenic	Brachycephaly, EEG abnormality, epicanthus, finger clinodactyly, flat occiput, intellectual disability, microcephaly, micrognathia, microtia, prominent antihelix, protruding tongue, short neck, short phalanx of finger, single transverse palmar crease, sparse hair
398081	46XY	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Abnormal dermatoglyphics, abnormality of cardiovascular system morphology, abnormality of the outer ear, blepharitis, brachycephaly, broad palm, depressed nasal bridge, epicanthus, hypotonia, protruding tongue, sandal gap, short neck, small hand, tetralogy of fallot, upslanted palpebral fissure
393936	46XX	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Downslanted palpebral fissures, EEG abnormality, finger clinodactyly, hypertonia, low-set ears, macrotia, micrognathia, primary microcephaly, prominent nasal bridge, short stature, small for gestational age, supernumerary ribs, wide nasal bridge
395590	46XX	21:41106204-46699983	5.59 Mb	De novo, mosaic	Likely pathogenic	Atresia of the external auditory canal, epicanthus, facial asymmetry, hypertelorism, intellectual disability, low-set ears, microcephaly, micrognathia, preauricular skin tag, proportionate short stature, sacral dimple, wide mouth
393891	46XY	21:41106204-46699983	5.59 Mb	De novo	Likely pathogenic	Abnormality of the skin, curly eyelashes, hypotonia, long eyelashes, low-set ears, micrognathia, narrow palate, peters anomaly, sclerocornea, small for gestational age, thin skin, wide intermamillary distance
396749	46XY	21:41106203-46699983	5.59 Mb	Unknown	Likely pathogenic	Abnormality of the pinna, EEG abnormality, highly arched eyebrow, hypertelorism, intellectual disability, macrotia, mandibular prognathia, proportionate short stature, protruding ear, thick lower lip vermilion, varicose veins, wide mouth
105	46XX	21:37784110-42396111	4.61 Mb	Unknown		Hallux valgus, intellectual disability, macrodontia, microcephaly, narrow forehead, prominent nose, seizure, short palm, short philtrum, stereotypy, wide mouth
251573	46XY	21:45714068-45755268	41.20 kb	Inherited from normal parent		Constipation, deeply set eye, delayed speech and language development, intellectual disability, microcephaly, proportionate short stature, short foot, short palm, spasticity, strabismus, wide nasal bridge
395566	46XX	21:41106204-46699983	5.59 Mb	De novo, mosaic	Likely pathogenic	Abnormal thrombocyte morphology, cleft palate, depressed nasal bridge, frontal bossing, hearing impairment, intellectual disability, non-midline cleft lip, proportionate short stature, talipes equinovarus, ventricular septal defect, wide nasal bridge
395577	46XY	21:41106204-46699983	5.59 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Brachycephaly, frontal bossing, hypoplasia of the maxilla, hypotonia, intellectual disability, microdontia, nystagmus, scoliosis, thin upper lip vermilion, upslanted palpebral fissure
393913	46XX	21:41106204-46699983	5.59 Mb	De novo, mosaic	Likely pathogenic	Anteverted nares, high palate, hypertonia, low-set ears, micrognathia, overlapping fingers, posteriorly rotated ears, prominent antihelix, prominent occiput, wide nasal bridge
401718	46XX	21:41599278-46677461	5.08 Mb	De novo	Likely pathogenic	Abnormality of finger, abnormality of the pinna, aplasia/hypoplasia of the earlobes, conductive hearing impairment, hypopigmentation of hair, long thorax, nystagmus, short neck, stenosis of the external auditory canal, vertebral segmentation defect
393875	46XX	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Cariou teeth, downslanted palpebral fissures, EEG abnormality, facial asymmetry, genu valgum, microcephaly, proportionate short stature, secondary amenorrhea, talipes equinovaglus
308310	46XY	21:40520005-46142503	5.62 Mb	Unknown		Anteverted nares, delayed speech and language development, downslanted palpebral fissures, generalized neonatal hypotonia, low-set ears, macrotia, mild global developmental delay, pes planus, prominent fingertip pads
394110	46XY	21:30205811-46699983	16.49 Mb	De novo, mosaic	Likely pathogenic	Abnormal immunoglobulin level, abnormal thrombocyte morphology, dolichocephaly, epicanthus, frontal bossing, high anterior hairline, intellectual disability, pili torti, recurrent infections
396772	46XY	21:30205811-46699983	16.49 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Intellectual disability, low-set ears, micrognathia, primary microcephaly, prominent nose, short neck, short stature, small for gestational age
392570	46XY	21:30205811-46699983	16.49 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Brachycephaly, cleft palate, intellectual disability, low-set ears, non-midline cleft lip, placental infarction, small for gestational age, small placenta
395541	46XY	21:41106204-46699983	5.59 Mb	De novo	Likely pathogenic	Depressed nasal ridge, downslanted palpebral fissures, epicanthus, facial asymmetry, intellectual disability, posteriorly rotated ears, short nose
396753	46XX	21:41106203-46699983	5.59 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Abnormality of the skin, delayed speech and language development, EEG abnormality, flat occiput, gait disturbance, hyperactivity, intellectual disability
359530	46XX	21:41785816-46670405	4.88 Mb	De novo	Pathogenic	Cleft palate, conductive hearing impairment, delayed speech and language development, impaired pain sensation, intellectual disability, recurrent infections
341696	46XX	21:42336476-46673449	4.34 Mb	Unknown		Cataract, cervical c2/c3 vertebral fusion, delayed speech and language development, episodic vomiting, lingual thyroid, toe walking
278295	46XY	21:46141745-46164939	23.20 kb	Maternally inherited	Likely benign	Abnormal external genitalia, behavioral abnormality, delayed speech and language development, global developmental delay, sleep disturbance
390415	46XY	21:40296018-46567246	6.27 Mb	Unknown	Pathogenic	Intellectual disability, polymicrogyria, scoliosis, seizure
367443	46XX	21:43071168-46664244	3.59 Mb	Unknown	Pathogenic	Cleft lip, delayed puberty, short stature, specific learning disability
386959	46XY	21:36423932-46648012	10.22 Mb	Unknown	Pathogenic	Abnormal heart morphology, hypospadias, intellectual disability, scoliosis
304201	46XY	21:38208527-46699983	8.49 Mb	Unknown	Likely pathogenic	Abnormal facial shape, mild receptive language delay, pectus excavatum, unilateral cleft palate
394149	46XY	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Proportionate short stature, upslanted palpebral fissure, ventricular septal defect
331338	46XY	21:44054543-45378292	1.32 Mb	Unknown	Likely pathogenic	Intellectual disability, mild, skeletal dysplasia, spastic paraparesis
395587	46XY	21:41106203-46699983	5.59 Mb	De novo, mosaic	Likely pathogenic	Intellectual disability, microcephaly, short neck
393955	46XY	21:41106203-46699983	5.59 Mb	De novo, mosaic	Likely pathogenic	Inguinal hernia, intellectual disability, microcephaly
414037	46XY	21:43094948-46670405	3.58 Mb	De novo	Pathogenic	Hypotonia, intellectual disability, scoliosis
350149	46XY	21:44057842-44064432	6.59 kb	Maternally inherited	Likely benign	Behavioral abnormality, intellectual disability, obesity
322809	46XY	21:46511395-46603068	91.67 kb	Unknown	Uncertain	2-3 toe syndactyly, abnormality of canine, intrauterine growth retardation
395505	46XY	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Decreased testicular size, oligospermia
393870	46XY	21:41106204-46699983	5.59 Mb	Imbalance arising from a balanced parental rearrangement	Likely pathogenic	Cryptorchidism, delayed puberty
294509	46XY	21:44059454-46636538	2.58 Mb	Unknown	Pathogenic	Cognitive impairment, oligospermia
260427	46XY	21:44253374-44282764	29.39 kb	Inherited from normal parent		Autism, intellectual disability
366645	46XY	21:42955906-46648012	3.69 Mb	Unknown	Pathogenic	Autism, global developmental delay
386963	46XY	21:41855368-43204628	1.35 Mb	Unknown	Uncertain	Unilateral cleft lip
395504	46XY	21:41106204-46699983	5.59 Mb	De novo	Likely pathogenic	Umbilical hernia
289193	Unknown	21:46517395-46621026	103.63 kb	Unknown	Likely benign	Primary amenorrhea
378976	46XY	21:41855368-43204628	1.35 Mb	Unknown	Uncertain	Oral cleft
393866	46XY	21:41106203-46699983	5.59 Mb	De novo	Likely pathogenic	Oligospermia
410231	46XX	21:44720054-45262269	542.22 kb	Unknown	Uncertain	Microcephaly
384325	46XX	21:44416925-46671337	2.25 Mb	De novo	Uncertain	Hypoplastic left heart