Supplementary Material Table of female patients who harbored truncating mutations and deletions in *AMER1*, and whose phenotype was thoroughly described in the literature

Patient	Variant	Zygosity	Inheritance	Sex	Dysmorphic features	Skeletal abnormalities	Neuromuscular abnormalities	Cardiovascular abnormalities	Respiratory abnormalities	Sensorineural abnormalities	Development hits	Other abnormalities	Source
1	c.194del p.Gly65Valfs*35	Het	de novo	F	Macrocephaly | Frontal bossing | Bifid uvula | short stature	Skull sclerosis | Metaphyseal striations of the long bones				Hearing impairment	Global developmental delay	Recurrent otitis media	Enomotoet al 2017
2	c.429T > A; p.(Cys143*)	Het	NA	F	Macrocephaly | Long face | Long philtrum | Thin lips | Narrow palate	Scoliosis | Metaphyseal striations of the long bones							Perdu et al 2011
3	c.337delG; p.(Gly113fs58*)	Het	NA	F	Macrocephaly | Frontal bossing | Dolichocephaly |Deep-set small eyes | Epicanthus | Hypertelorism | Broad nasal bridge |Low-set ears | High arched | Narrowpalate | Microretrognathia	Skull sclerosis | Bilateral knee contracture | Metaphyseal striations of the long bones | Thoracolumbar gibbus	Poor head control | Ventriculomegaly | Megacisterna magna | Migraine			Hearing impairment	Global developmental delay | Dentition delay	Intestinal malrotation	Perdu et al 2010
4	c.555_556delTG; p.(Ala187*)	Het	De novo	F	Macrocephaly | Cleft palate | Prominent Forehead | Retrognathia | Anteverted nares | Clinodactyly | Hypertelorism | Epicanthus | Wide nasal bridge	Metaphyseal striations of the long bones	Ventriculomegaly | Polyhydramnios			Hearing impairment	Intellectual disability, mild | speech delay	Wilms tumor	Sperotto et al 2017
5	c.811C > T; p.(Gln271*)	Het	Inherited from mother	F	Macrocephaly | Cleft palate | Hypertelorism | Pectus excavatum	Skull sclerosis |Left maxillary hypoplasia | Metaphyseal striations of the long bones		Mitral valve insufficiency/stenosis		Hearing impairment			Koenig et al 1996
6	c.811C > T; p.(Gln271*)	Het	Inherited from mother	F	Macrocephaly | Hypertelorism | Broad nasal bridge | Maxillary hypoplasia | Prominent mandible | Low-set ears | Dysplastic ears	Skull sclerosis |Left maxillary hypoplasia | Metaphyseal striations of the long bones, ribs and scapulae	Hydrocephalus	Atrial septal defect | Patent ductus arteriosus					Koenig et al 1996
7	c.811C > T; p.(Gln271*)	Het	Inherited from mother	F	Macrocephaly | Hypertelorism| Broad nasal bridge	Skull sclerosis | Metaphyseal and diaphyseal striations of the long bones and jaw | Thickened calvarium							Koenig et al 1996
8	c.811C > T; p.(Gln271*)	Het	Inherited from mother	F	Macrocephaly	Skull sclerosis | Metaphyseal striations of the long bones					Speech delay		Koenig et al 1996
9	c.654delG; p.(Asp216fs62*)	Het	NA	F	Large forehead | Hypertelorism |Flat face | Highly arched palate| Broad nasal bridge	Skull sclerosis | Thickened calvarium | Metaphyseal striations of the long bones				Hearing impairment			Perdu et al 2011
10	c.827_842del16; p.(Pro276Glnfs*13)	Het	Germline mosaicism	F	Macrocephaly | Micrognathia |Cleft palate | Dysplastic ear | Wide anterior fontanelle | frontal bossing	Striations of the ribs | Metaphyseal striations of the long bones | skull sclerosis	Ventriculomegaly | Hypotonia	Atrial septal defect	Severe upper airway compromise	Hearing impairment	Normal		O'Byrne et al 2016
11	c.956_957insT; p.Lys320Glufs*4	Het	de novo	F	Macrocephaly | Prominent forehead | Dolichocephaly | Persistent open anterior fontanelle | Retromicrognathia | Narrow palate | Bifid uvula | Hypertelorism | Epicanthus | Slanting palpebral fissures | Low-set ears | Broad nasal bridge | Long philtrum	Skull sclerosis | Metaphyseal and diaphyseal striations of the long bones and jaw | talipes valgus	Hypotonia | Ventriculomegaly	Left ventricular hypertrabeculation	Tachypnea | pneumothorax		Speech delay		García-Aznar et al 2019

(*Continued*)

Supplementary Material (*Continued*)

Patient	Variant	Zygosity	Inheritance	Sex	Dysmorphic features	Skeletal abnormalities	Neuromuscular abnormalities	Cardiovascular abnormalities	Respiratory abnormalities	Sensorineural abnormalities	Development hits	Other abnormalities	Source
12	c.1045C > T; p.(Gln349)	Het	De novo	F	Macrocephaly | Frontal bossing | Widely spaced eyes | Blepharophimosis | Microtia | Posteriorly rotated low-set ear | Overfolded helix | Broad nasal bridge | Small nose | cleft palate | Micrognathia	Wide anterior fontanelle | Delayed bone age | skull sclerosis	Ventriculomegaly | Hypoplasia of the corpus callosum | Mild muscle weakness in low extremities	Ventricular septal defect			Developmental delay | Speech delay	Hepatoblastoma	Fujita et al 2013
13	c.1057C > T; p.(Arg353*)	Het	Inherited from mother	F	Mild macrocephaly | Narrow forehead |Frontal bossing | Hypertelorism | Epicanthal folds | Slanting palpebral fissures | Depressed nasal | Hypoplastic maxillae | Low-set ears | Pectus excavatum | High-arched palate | Dental-position abnormalities	Skull sclerosis | Striations in the pelvis | Metaphyseal striations of the long bones				Hearing impairment	Delayed dentition | Global developmental delay		Zicari et al 2012
14	c.1057C > T; p.(Arg353*)	Het	NA	F	Hypertelorism | Epicanthal folds | Depressed nasal | Hypoplastic maxillae	Metaphyseal striations of the long bones							Zicari et al 2012
15	c.1072C > T; p.(Arg358*)	Het	NA	F	Frontal bossing | Bitemporal narrowing, tooth malpositioning | Hypotelorism	Skull sclerosis | Metaphyseal striations of the long bones | Otosclerosiss				Hearing impairment | Myopia		Recurrent otitis media	Jenkins et al 2008
16	c.1072C > T; p.(Arg358*)	Het	NA	F	Macrocephaly | Facial asymmetry | Prominent of the forehead | Epicanthus | Broad nasal bridge | Abnormal dentition	Skull sclerosis | Metaphyseal and diaphyseal striations of the long bones | Abnormal density of the jaw				Hearing impairment			Pellegrino et al 1997
17	c.1072C > T; p.(Arg358*)	Het	NA	F	Macrocephaly | Cleft palate | Frontal bossing | Deep-set eyes | Telecanthus | Broad nasal bridge	Skull sclerosis | Widened ribs	Hypotonia	Ventricular septal defect | Patent ductus arteriosus		Hearing impairment	Global developmental delay		Bueno et al 1998
18	c.1072C > T; p.(Arg358*)	Het	Inherited from father?	F	Macrocephaly | hypertelorism | frontal bossing | Anteverted nares | large mouth	Skull sclerosis | Metaphyseal striations of the long bones	Ventriculomegaly | Polyhydramnios | Hypotonia	Ventricular septal defect	Respiratory distress | Laryngomalacia	Hearing impairment	Global developmental delay		Ciceri et al 2013
19	c.1267delC; p.(Leu423fs25*)	Het	Inherited from mother	F	Macrocephaly | Flat nasal bridge |Frontal bossing | Hypertelorism	Thickened calvarium | Metaphyseal striations of the long bones | Bilateral fibula | Otosclerosis				Hearing impairment		Recurrent otitis media | Ovarian carcinoma	Keymolen et al 1997
20	c.1267delC; p.(Leu423fs25*)	Het	NA	F	Macrocephaly | Polydactyly | Large forehead | Hypertelorism | Ptosis	Skull sclerosis | Thickened calvarium | Metaphyseal striations of the long bones | Bilateral fibula | Otosclerosis	Paraparesis | Positive Babinski sign			Sensory impairment		Multiple sclerosis | Chronic sinusitis	Keymolen et al 1997
21	Whole gene deletion	Het	De novo	F	Macrocephaly | Coarse facies | Slanting of the palpebral fissure | Epicanthus inversus | Posteriorly rotated low-set ears | Folded helix | Macrotia | Wide nasal bridge | Anteverted	Flaring of theiliac wings | Widening ribs | Flattening vertebral bodies in the cervical and thoracic spine | Skull sclerosis | Abnormal head shape | Metaphyseal	Ventriculomegaly | Hypotonia | Colpocephaly | Hypoplasia of the corpus callosum	Ventricular septal defect | Pericardial effusion	Laryngotracheomalacia | Chronic lung disease	Hearing impairment	Developmental delay | Speech delay	Hirsutism | Pyloric stenosis | Dysphagia | Gastroesophageal reflux	Herman et al 2013

Supplementary Material (*Continued*)

Patient	Variant	Zygosity	Inheritance	Sex	Dysmorphic features	Skeletal abnormalities	Neuromuscular abnormalities	Cardiovascular abnormalities	Respiratory abnormalities	Sensorineural abnormalities	Development hits	Other abnormalities	Source
					nares | Hypoplastic nasal tip | Cleft palate	striations of the long bones							
22	Whole gene deletion	Het	Inherited from mother	F	Macrocephaly | Parietal bossing | Cleft palate | Syndactyly	Skull sclerosis | Metaphyseal striations of the long bones | Fibula osteolysis		Atrial and ventricular septal defects		Hearing impairment		Anterior ectopic anus | Left hydronephrosis | Dilated left ureter | Small right kidney	Savarirayan et al 1997
23	Whole gene deletion	Het	Inherited from mother	F		Thickening of the skull | Skull sclerosis | Metaphyseal striations of the long bones | Striations of the maxilla and mandible							Savarirayan et al 1997
24	Whole gene deletion	Het	NA	F	Macrocephaly | Cleft palate | Midface hypoplasia	Skull sclerosis | Metaphyseal striations of the long bones				Hearing impairment			Savarirayan et al 1997

Note: Phenotype description was adapted using the Human Ontology Phenotype terms.

Table of survival male patients who harbored truncating mutations in *AMER1* and whose phenotype was thoroughly described in the literature

Patient	Variant	Zygosity	Inheritance	Sex	Dysmorphic features	Skeletal abnormalities	Neuromuscular abnormalities	Cardiovascular abnormalities	Respiratory abnormalities	Sensorineural abnormalities	Development hits	Other abnormalities	Source
25	c.429T > A: p.(Cys143*)	Hem	Inherited from mother	M	Dolichocephaly | High forehead | Hypertelorism | Downslanting palpebral fissures | Mild ectropion of the eyelids | Broad nasal tip | bilateral cleft lip and palate | Dysplastic low-set ears | Hypodontia	Skull sclerosis | Short and broad clavicles | Bilateral proximal fibular hypoplasia | Broad thumbs and halluces | Flexion contractures of the fingers II–V | Scoliosis	Hypoplasia of the corpus callosum | Ventriculomegaly | Seizures | Arnold–Chiari I malformation	Atrial septal defect | Patent ductus arteriosus	Respiratory problems | Apnea	Hearing impairment	Global developmental delay	Umbilical hernia | Hypoplastic abdominal muscles	Perdu et al 2011
26	c.607_611delAGGCC; p.Arg203fs*2	Mos	Somatic mosaicism	M	Macrocephaly | Cleft palate | Cryptorchidism | Natal tooth | Wide anterior fontanel | Hypertelorism | Broad nasal bridge | Low-set ears | Micrognathia | Deep palmar Creases | Smooth philtrum	Skull sclerosis	Ventriculomegaly		Respiratory distress			Inguinal hernia | Gastrointestinal Reflux | Duplication of renal pelvis	Hague et al 2017
26	c.811C > T; p.(Gln271*)	Hem	Inherited from mother	M	Macrocephaly | Micrognathia | Cleft palate | Dolichocephaly | Frontal bossing | Mild hypertelorism | Broad nasal bridge | Dental malformations | Low-set ears	Skull sclerosis | Maxilla sclerosis | Metaphyseal striations of the long bones	Ventriculomegaly		Tracheomalacia	Hearing impairment			Koenig et al 1996
27	c.811C > T; p.(Gln271*)	Hem	Inherited from mother	M	Macrocephaly | Cleft palate | Frontal and occipital bossing | Epicanthic folds | Hypertelorism | Depressed nasal bridge | Full lips	Hip dysplasia			Malformation of the epiglottis | Recurrent obstructive sleep apnea				Koenig et al 1996
29	c.654delG; p.(Asp216fs62*)	Hem	Inherited from mother	M (fetus)	Relatively macrocephaly | Upturned nasal tip | Long philtrum | Micrognathia | Retrognathia | Low-set rotated posteriorly ears | Underdeveloped tongue	Bilateral fibula	NA	Hypoplastic left heart | Severe heart defect	NA	NA	NA	Intestinal malrotation	Perdu et al 2011
30	c.1072C> T; p.(Arg358*)	Mos	Germline mosaicism	M	Broad forehead | Hypertelorism | Epicanthus, wide nasal bridge | Low set ears	Skull sclerosis | Metaphyseal striations of the long bones | Scoliosis | Left club foot	Ventriculomegaly | Leucomalacia		Restrictive lung disease	Hearing impairment	Mild intellectual disability	Inguinal hernia	Holman et al 2011
31	c.1072C> T; p.Arg358*	Mos?	Germline mosaicism?	M	Yes (similar to his daughter)	Skull sclerosis | Metaphyseal striations of the long bones				Otosclerosis			Ciceri et al 2013
32	c.1108G > T; p.Glu370*	Mos	Mosaicism	M	Macrocephaly | hypertelorism | wide nasal bridge | Talipes equinovarus | Cleft lip | Cleft palate | prominent forehead | Micrognathia	Skull sclerosis | Metaphyseal striations of the long bones | Ankylosis				Hearing impairment	Mild intellectual disability		Joseph et al 2010
33	c.1275C > G; p.(Tyr425*)	Hem	Inherited from mother	M	Yes	Yes		Yes		Yes	Yes		Jenkins et al 2008
34	c.1267delC; p.(Leu423fs25*)	NA	NA	M	Macrocephaly | Cleft palate | Frontal bossing | Hypertelorism | Bilateral epicanthus | High arched palate |Micrognathia	Thickened calvarium				Hearing impairment	Speech delay	Severe stomach problems,	Keymolen et al 1997
35	c.1591C> T; p.(Arg531*)	NA	Inherited from mother	M	Broad forehead | Hypertelorism | Epicanthus | Wide nasal bridge	Skull sclerosis | Pes calcaneovalgus	Mild spastic diplegia	Accessory mitral valve tissue		Hearing impairment	Mild intellectual disability		Holman et al 2011
36	c.1506delA; p.(Gly502fs38*)	Hem	Inherited from mother	M	Yes	Yes					Yes		Jenkins et al 2008

Note: Phenotype description was adapted using the Human Ontology Phenotype terms.