Supplementally Table 1. Phenotypic varaibility of patients with *GLI2* deficiency

Patients with *GLI2* point mutations

Pt.#	Mutation	Mutation type	Inheritence	Brain image	Pituitary gland	Anterior Pituitaly function	Intellecutal disability	Polydactyly	Cleft lip/palate	Cranio-Facial	Others	Ref.
1	p.Trp113*	nonsense	parental gonadal mosaicism	N	pituitary hypoplasia	GH def	ND	postaxial hexadactyly	Bilateral cleft lip and palate	microcephaly, hypotelorism, single central incisor.		1
2	DNA was not available		parental gonadal mosaicism	alobar HPE, hydrocephalus	absent AP	ND	ND	N	N	hypotelorism, single nostril, hypoplastic palate and maxilla.	sister of Pt.1	1
3	IVS5+1G>A	splicing	from father	N	ND	GH def: severe growth retardation	developmental delay	N	pseudomedian cleft lip	hypotelorism, single nares, extreme midface hypoplasia, microcephaly.		1
4	IVS5+1G>A	splicing		ND	ND	ND	N	N	N	apparently normal.	father of Pt.3	1
5	p.Arg168*	nonsense	from father	referred with HPE findings	ND	ND	ND	ND	ND	ND		1
6	p.Arg168*	nonsense		ND	ND	ND	N	N	N	apparently normal.	father of Pt.5	1
7	c.2274del1	frame shift	from father	optic nerve hypoplasia,	absent pituitary on MRI	pan-hypopituitarism	ND	bilateral postaxial polydactyly	Repaired cleft lip and palate	ND		1
8	c.2274del1	frame shift	from father	abnormal configuration of lower midline structures, and partial agenesis of the corpus callosum by head ultrasound.	absent pituitary	pan-hypopituitarism	ND	ND	midline cleft lip and palate	hypotelorism, flat midface.	twin brother of Pt.7	1
9	Deceased			ND	ND	pan-hypopituitarism	ND	ND	ND	ND	twin brother of Pt.7, One sibling died at 5 months of age.	1
10	c.2274del1	frame shift		ND	ND	ND	N	postaxial polydactyly	ND	ND	father of Pt.7	1
11	c.2274del1	frame shift		ND	ND	ND	N	postaxial polydactyly	ND	ND	paternal aunt of Pt.7	1
12	p.Arg151Gly	missense	from normal mother	N	N	GH def: height 25th	N	N	Cleft lip/palate	small frontonasal angle, hypotelorism, hypoplastic nose, hypoplastic nasal septum, hypoplastic. midface, small philtrum		2

13	p.Arg151Gly	missense	ND	mild gyral asymmetry in the perisylvian areas	ND	ND	N	N	bilateral cleft lip/palate	large ears, hypoplastic anterior nasal spine, diminished frontonasal angle, hypotelorism, hypoplastic premaxilla, hypoplastic nose with flattened alae and nasal tip, poorly developed philtrum, malocclusion.	Also has PTCH1, p.Thr328M	3
14	p.Pro1226Leu	missense	ND	ACC, abnormal development of the ventricular frontal horns, and an abnormal gyral pattern	N	ND	severe mental retardation	N	bilateral cleft lip/palate	hypotelorism, epicanthic folds, malar hypoplasia, broad and poorly developed nasal tip, prominent lower lip.		3
15	p.Pro604Ser	missense	ND	agenesis of the right eyeglobe, ACC, asymmetric ventricles, migrational defects mainly in the right hemisphere, and abnormal	N	ND	ND	N	N	a small occipital meningocele, prominent forehead, large anterior fontanel, right-sided anophthalmia, small abnormally modeled and posteriorly angulated ears, preauricular tags, wide downturned mouth, short neck.		3
16	p.Met1116Ile	missense	ND	ND	ND	ND	ND	N	N	prominent forehead, asymmetric face, small left orbit, ptosis of the eyelids, marked left heminasal hypoplasia with a small pit in the nasolacrimal region, mild retroposition of the left ear, open bite.	CT scan disclosed atresia of the left choana, hypoplasia of the left frontal and maxillary sinuses, abnormal pneumatization. of the right paranasal sinus, and mild left-sided septal deviation	3
17	c.2362_2368del	frame shift	from mother with polydactyly	N	hypoplastic AP, ectopic PP	GH,TSH,ACTH,LH/FSH def	Y	Y	N	ND		4
18	c.2081_2084del	frame shift	from normal father	N	hypoplastic AP, ectopic PP	GH def: height -4.5SD, partial ACTH def	N	N	cleft lip and palate	flat nasal bridge		4

19	p.Glu380*	nonsense	from noraml mother	N		hypoplastic AP,absent PP	GH def: height (-2.9SD), TSH,ACTH,ADH def	severe developmental delay	N	N	ND	4
20	p.Ala268Val	missense	ND	N		ND	ND	N	N	right cleft lip with preserved palatal structures	high forehead, flat facial profile, low nasal bridge, broad nasal ridge, hypoplastic nasal septum, abnormal and short philtrum, short columella.	5
21	p.Ser1555Pro	missense	from mother with hypoteloris m	N		N	ND	N	right hand preaxial polydactyly	bilateral cleft lip/palate	flat face, maxillary hypoplasia, arched eyebrows, down slanted palpebral fissures, epicanthus inversus, large ears, low nasal bridge, flat nose, hypoplastic columella and philtrum.	5
22	c.1530_1531insC	frame shift	from mother with polydactyly	N		N	ND	N	bilateral surgical scars from postaxial polydactyly correction.	surgically corrected midline cleft	long and flat profile, hypotelorism, broad nasal tip, wide nasal cavity, hypoplastic septum, thin columella, long philtrum, agenesis of the premaxilla.	5
23	c.864_866del	inframe deletion	from mother with polydactyly	Brain MRI showed semilobar holoprosencephaly.		N	ND	severe neurodevelop mental delay	bilateral postaxial polydactyly	large cleft lip/palate involving partially the premaxilla,	microcephaly	5
24	p.Glu629Lys	missense	ND	N		ND	ND	N	N	N	high forehead, facial asymmetry with hypoplastic right side, right epibulbar dermoid, thin and asymmetric nose, bilaterally abnormally modeled ears with preauricular skin tags, Tessier cleft number 7 at right, and short neck.	5

25	p.Asp1520Asn	missense	de novo	N	ND	ND	N	N	N	high forehead, facial asymmetry with hypoplastic left side, left-sided anophthalmia, abnormally modeled ears, bilateral preauricular skin tags greater at left, and Tessier cleft number 7 at left.		5
26	c.1908dupC	frame	ND	ND	ND	GH def	ND	Y	ND	ND	ASD, VSD	6
27	p.Gln925*	nonsense	ND	ND	aplasia of pituitary	ND	ND	Y	ND	ND		6
28	p.Gln925*	nonsense	ND	ND	empty sella	panhypopituitarism	ND	Y	ND	ND		6
29	c.3294_3295del	frame shift	ND	ND	aplastic AP	panhypopituitarism	ND	Y	ND	ND		6
30	c.3555delC	frame shift	from normal mother	ND	pituitary hypoplasia, Chiari1	panhypopituitarism	ND	ND	ND	single central incisor		6
31	p.Gln1128*	nonsense	ND	ND	small AP, ectopic PP	panhypopituitarism	Y	Y	N	ND		6
32	p.Gln1128*	nonsense	ND	ND	small AP, ectopic PP	panhypopituitarism	Y	Y	ND	ND		6
33	p.Val183Met	missense	from normal father	ND	small AP, ectopic PP	GH def	ND	ND	ND	ND		6
34	p.Gln1256*	nonsense	from father with polydactyly	ND	empty sella	panhypopituitarism	ND	Y	ND	ND		7
35	p.Gln1256*	nonsense		ND	pituitary aplasia	ND	ND	Y	ND	ND	Nephew of Pt.34, PDA	7
36	p.Pro253Ser	missense	ND	ND	small AP, ectopic PP	GH,TSH,ACTH def	ND	ND	ND	ND		8
37	p.Arg516Pro	missense	from normal father	ND	small AP, ectopic PP	GH,TSH,LH/FSH def	ND	Y	ND	ND		9
38	p.Glu518Lys	missense	ND	ND	hypoplastic AP,absent PP, normal pituitary stalk and hypothalamus	GH, TSH def	normal cognition with social/behavioural problems	ND	ND	ND		10

39	p.Arg720His	missense	ND	ND	small AP with no structural abnormality	GH,LH/FSH def	ND	ND	cleft palate	ND		Klippel–Feil syndrome; short neck and cervical vertebral fusion leading to limited movement. Bilateral sensorineural hearing loss. Left sided Sprengel deformity and right-sided	10

Patients with chromosomal deletions including *GLI2* locus

Pt.#	Deletion	Methods	Inheritence	Brain image	Pituitary gland	Postnatal growt retardation	Intellecutal disability	Polydactyly	Cleft lip/palate	Cranio-Facial	Others	Ref.
40	2q14.2 (1.3Mb)	CMA, MLPA	from father	ND	pituitary anomaly	Y	N	N	bilateral cleft lip and palate	ND	Heterotaxy	11
41	2q14.2-22.1 (20Mb)	CMA, FISH	de novo	ND	ND	N	N	left hand postaxial polydactyly	ND	ND	hypospadias, double-left sided ureteres, undescended testes, exotropia and amblyopia of the left eye. Post operative deep vein thrombosis.by protein C deficiency.	12
42	2q14.2-21.3	CMA	de novo	ventriculomegaly	ND	ND	Y	N	N	single central incisor	prenatal Dx	13
43	2q14.1-22.1 (19Mb)	CMA	de novo	N	ND	Y: height <0.4th centile at 20mo	Y: walking, no word at 3-year old.	a skin tag on the left 5th finger.	N	wide anterior fontanelle extending into the metopic suture, a high, domed forehead, bitemporal narrowing, prominent sagittal sutures, sparse eyebrows, deep-set eyes, flat nasal bridge, horizontal creases on the nasion, broad and prominent nasal tip, marginally low-set ear swith posterior rotation, micrognathia.	The pregnancy was complicated by significant vaginal bleeding at 6 weeks of gestation and by pre-eclampsia at 33 weeks of gestation. Apgar scores were 9 and 10. Congenital right talipes equinovarus, PDA,PFO.	14
44	2q14.2q14.3 (4.3Mb)	CMA	from father	abnormal temporal myelinization.	ND	GH def:150 cm woman (-2.47 SD) at 25-year old.	N	N	ND	high anterior hairline, short philtrum, pointed chin, long nose, esotropia.	VSD, ASD, scoliosis, left kidney was removed because it was nonfunctional and multicystic.	15
45	2q14 (5.8Mb)	CMA	from mother	ACC	ND	Y	Y: mild	N	N	high forehead, broad nasal bridge, down slanting palpebral fissures, low-set ears, anteverted nares, long philtrum with a tented upper lip, and		16
46	2q14	CMA	from mother	ND	ND	Y	Y	ND	ND	similer to Pt.6	brother of Pt.45	16
47	2q14.2 (0.12Mb)	CMA	from mother	Chiari 1 malformation	ectopic PP	Y	ND	right hand postaxial polydactyly	N	Mild midface hypoplasia		17

48	2q14.2 (0.12Mb)	CMA	from mother	ND	ND	Y	ND	bilateralhand postaxial polydactyly	N	ND	sister of Pt.47	6
49	2q14.1q14.3 (6.6Mb)	CMA	de novo	N	ND	Y	Y: mild	N	Y	flat nasal bridge	selective mutism	Present case
50	2q12q14	GTG	de novo	ACC	ND	Y	Y: severe	Y	Y	facial dysmorphism, short neck	VSD, hydronephrosis, i	18
51	2q14q21	GTG	de novo	N	ND	ND	N	N	N	bulging forehead, hypertelorism, downward slanting palpebral fissures, low set ears and a short nose with broad flattened nasal bridge.		19
52	2q14q21	GTG	ND	ACC	ND	ND	Y: severe	N	N	enophthalmos, long philtrum, micrognathia, narrow forehead, prominent glabella, and depressed nasal bridge.	PDA, tendency to severe pyogenic infections, , unilateral corneal clouding, with Peterslike anomaly.	20
53	2q13q21	GTG	de novo	ACC, Dandy-Walker	ND	Y	Y: severe	N	N	ND	Heterotaxy, Large ASD	21
54	2q14.1q21	GTG, FISH	from father	ND	ND	N	Y: mod, ADHD	N	N	high forehead, prominent mandible, low set and dysplastic with some overfolding ears, high arched palate.	mild aortic root dilatatic	22
55	2q21q24	GTG	ND	ND	ND	Y	Y: severe	N	Y	ND	PDA	23
56	2q22q31	GTG	ND	ND	ND	ND	ND	N	Y	mimicking trisomy 18 phenotyp	Truncus arteriosus	24
57	2q13q21	GTG, MS	de novo, paternal del	N	ND	GH def	Y: walking at 3 years, speak two-word sentensces at 6 years.	bilateral postaxial hexadactyly	N	large, dysplastic low set ears, upsweep of anterior hairline, downslanting palpebral fissures, prominent mandible.		25
58	2q14	GTG	ND	ND	ND	Y	Y	N	ND	ND		26

Abbreviation: ACC = agenesis of corpus callosum, AP = anterior pituitary, ASD = atrial septal defect, CMA = chromosomal microarray, FISH = fluorescence in situ hybridization, MS = microsatellite analysis, GTG = trypsin and Giemsa produce G-banding, MLPA = multiplex ligation-dependent probe amplification, N = normal, ND = not described, PDA = patent ductus arteriosus, PFO = patent foramen ovale, PP = posterior pituitary, Y = positive

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