Supplementary Table 1b: Clinical Details of Individuals with FBXO11 variants											
	P11	**P12**	**P13**	**P14**	**P15**	**P16**	**P17**	**P18**	**P19**	**P21**	**P22**
Gender	Male	Male	Male	Female	Female	Male	Male	female	female	male	Female
Age at last investigation	5.5 years	12y4m	9y	11 years	13 years 10months	20 years old	23 years	7 years	13	2 years 9 months	9 years 6 months
variant description NM_001190274.1	c.2636_2637delAG (p.Glu879Valfs*3)	deletion exons 12-23 plus MSH6	c.1649_1651del p.(Gly550del)	c.2626C>T (p.His876Tyr)	deletion exon 18	c.1655A>T; p. Y552F	c.1714G>T p.(Ala572Ser)	deletion exons 1-11	deletion exons 1-11	*FBXO11* whole gene deletion and *MSH6* partial deletion exons 2-9	c.2015dup; p.(Ser672Argfs*6))
Methods	trio ES	trio GS	trio ES	trio ES	duo GS	ES	trio ES	trio GS	trio ES	Array	trio GS
Inheritance/ De novo?	de novo	de novo	de novo	de novo	unknown	denovo	denovo	denovo	denovo	denovo	denovo
ACMG criteria	PS4, PVS1, PM2, PM6	2A-2E +0.9, 4L-4O +0.15	PS4, PM4, PM5, PM2,PM6	PM2, PP3, PP2, PM6	2A-2E +0.9	PM2, PP2, PM6	PM2, PM1, PP2, PM6	2A-2E, 4L	2A-2E, 4L	2A-2E, 4L-4O	PVS1, PM2, PM6
ACMG classification	pathogenic	pathogenic	pathogenic	likely pathogenic	likely pathogenic	variant of uncertain significance	Likely pathogenic	pathogenic	pathogenic	pathogenic	pathogenic
Contributor classification	likely pathogenic	pathogenic	pathogenic	likely pathogenic	likely pathogenic	Likely pathogenic	pathogenic	pathogenic	pathogenic	pathogenic	pathogenic
Other variants	N/A	MSH6 deletion	N/A	PAX6 variant	N/A	N/a	N/a	N/A	N/A	N/A	N/A
B. weight	2.86 kg (-1.12SD)	2.82 kg (-1.19SD)	3.15kg (-0.66SD)	2.60 kg (-1.57SD)	2.10kg (-2.52SD)	NA	3.4 kg (-0.26SD)	2.59kg (-1.59SD)	4.2 kg (+1.69SD)	1.22kg	2.59kg
B. weight (SD)	-1.12	-1.19	-0.66	-1.57	-2.52	NA	-0.26	-1.59	1.69	-1	-1.76
B. length	48 cm (-0.81SD)	48 cm (-0.81 SD)	50 cm (-0.06SD)	47cm (-1.10SD)	42 cm (-3.34SD)	NA	51.5cm (+0.51SD)	47cm (+1.10SD)	54cm (+1.65SD)	38cm	46cm
B. length (SD)	-0.81	-0.81	-0.06	-1.1	-3.34	NA	0.51	1.1	1.65	-0.67	-1.55
B. OFC	N/A	34 cm (-0.83 SD)	35.5 cm (-0.18SD)	31cm (-2.58 SD)	N/A	NA	34cm (-0.83SD)	33cm (-1.22SD)	35cm (0.11SD)	27cm	32cm
B. OFC (SD)		-0.83	-0.18	-2.58		NA	-0.83	-1.22	0.11	-1.5	-1.9
Weight	14.97 kg (-2.07SD)	65 kg (+2.1SD)	23 kg (-1.59SD)	140 cm (0 SD)	55kg (+0.38SD)	45 kg (-2.84SD)	91kg (+1.37SD)	28kg (+0.96SD)	71kg (+1.81SD)	13kg	41.8kg
Weight (SD)	-2.07	2.1	-1.59	0	0.38	-2.84	1.37	0.96	1.81	-0.64	1.3
Height	102 cm (-1.89SD)	155 cm (+0.78SD)	129cm (-0.74SD)	49 cm (-2,8 SD)	144 (-2.5SD)	125cm (-7.17SD)	172cm (-0.64SD)	123cm (+0.27SD)	172cm (+2.18SD)	91.5cm	140cm
Height (SD)	-1.89	0.78	-0.74	-2.8	-2.5	-7.17	-0.64	0.27SD	2.18	-0.55	0.79
OFC	N/A	54.5cm (+0.49SD)	51.5 cm (-0.78SD)	N/A	50 cm (-3.2 SD)	49cm (-4.1SD)	56cm (+0.63SD)	50cm (-1.14SD)	56cm (1.88SD)	45	52cm
OFC (SD)		0.49	-0.78		-3.2	-4.1	0.63	-1.14	1.88	-2.7	0.04
Walking at age	24 months	17 months	24 months	17 months	24 months	16 months	12months	16 months	23 months	19 months CGA	17 months
first words at age/speech abilities	24 months	speech delay then improvement to normal ability	3 years	simple sentences at 6 years	first words at 24months	13 months	2 years	3 years	2 years	10 months CGA then plateaud, now improving with speech therapy	moderate to severe delay
DD/ID severity	Mild	mild	mild	mild	moderate	yes, severe	mild/moderate	mild	mild ID	mild fine motor delay and broderline lagnuage delay	severe motor coordination impairment, Developmental coordination disorder
IQ/DQ	N/A	heterogenous profil : VCI=62, VSI=72, FRI=74, WMI=82, PSI=60	N/A	N/A	N/A	51	N/A	borderline IQ	mild ID	mild GDD	mild
any regression	no	no	no	no	no	no	no	no	no	no	no
Seizures (onset) (type)	no	no	one episode	no	2 years, generalised epilepsy	generalised	myoclonic	no	no	1 seizure	yes
MRI anomalies	N/A	bilateral temporal gliosis	medial temporal white white matter changes	no	no		no	no	no	periventircualr leukomalacia	no
Hypotonia	Yes	Yes	Yes	no	Yes	yes	no	no	no	no	yes
Sleeping difficulties	no	no	no	no	Yes	yes	no	no	no	very poor sleep, resistive to sleep onset	yes, takes melatonin
Behavioural anomalies	no	slowness of execution, emotional inhibition	autism spectrum disorder	no	no	aggression	no	no	no	nil	autism, ADHD, sensory-seeking behaviours and inattention remain prominent affecting learning and information retention
Cardiac Malformations	N/A	no	Yes	no	no	no	no	heart murmur	no	PDA - closed	no
Renal malformation	N/A	no	no	no	no	no	no	no	no	no	no
Genital malformation	N/A	no	bilateral undescended testis	no	no	no	no	no	no	no	no

vision	Normal	Normal	refractory error, hypermetropia	aniridia	Normal	normal	myopia and astigmatism	normal	no	no	divergent squint
hearing	Normal	Normal	Normal	Normal	N/A	normal	normal	normal	no	mild conductive hearing impairment, improved with	no
microcephaly	Yes	no	no	Yes	Yes	yes	no	no	no	yes	no
dental	Normal	thick gingiva	dental abscess	N/A	N/A	normal	no	no	no	no	early loss of premature and early eruption of adult teeth
nose	normal	large	depressed nasal bridge	N/A	large	broad nasal bridge	no	no	no	no	no
philtrum	Normal	N/A	long	N/A	short	large	short	no	no	flattish philtrum	long
other	N/A	spontaneous mouth opening protruding tongue when little	epicanthus	thin upper lip	large mouth, synophyrys	no	synophyrys	no	no	thin upper lip, prominent ears, upIsalnting palpebral fissures, pointed chin	jowly face, synophyrys, round face
Abnormalities of hands and feet	no	Brachydactyly and finger anomalies with absent flexion of distal interphalangeal joint	no	Brachydactyly	Brachydactyly	no	no	no	no	no	no
Cleft lip or palate	no	no	no	no	no	no	no	no	no	no	no
Skeletal anomalies	no	N/A	hyperextensibility, bilateral Perthe's disease	no	no	no	no	no	no	no	no
recurrent infections/otitis media	no	no	no	no	no	recurrent chest infections	no	no	no	otitis media nad recurrent respiratory tract infections	yes
Other anomalies	No	hyperhidrosis	chronic diarrhoea	hyperhidrosis	hyperhidrosis	no	no	no	no	no	precocious puberty