

Supplementary Table 3. Review of all *KMT2B*-related dystonia in Asian population

Study (yr)	Case No.	Variant details	Variant type	Variant classification	Inheritance	Age (yr)	Sex	Country	Family history	AAO (yr)	Phenotype	Site of onset	Body parts involved	Time to generalization (yr)	Developmental abnormality or systemic findings/ID	Facial dysmorphism	Microcephaly	Psychiatric symptoms	Short stature	Additional features	Brain MRI	Medical management	DBS (Yes/ No) (BFMDRS-M/D pre and post-DBS)
Zhou et al., ¹ 2019	67	c.4789C>T(p.Arg1597Trp)	Missense	LP	De novo	19	F	China	Nil	4	Generalized dystonia	RLL	BLL, BUL, trunk	11	Normal	Bulbous nose tip	No	Nil	No	Nil	Normal	NA	No
Kawara et al., ² 2018	68	c.309delG	Deletion	Not reported	De novo	16	F	Japan	Nil	6	Generalized dystonia	Trunk, UL, LL	Face, trunk, BUL, BLL < larynx	< 1	Normal	Bulbous nose tip, elongated facies	Yes	Nil	Yes	Choreoathetoid movements	Normal	NA	Yes (47.5/- to 14/-)
	69	c.1656dupC	Duplication	Not reported	De novo	22	M	Japan	Nil	8	Generalized dystonia	RUL	Trunk, neck, BUL, BLL	NA	Yes	Normal	Yes	Nil	Yes	Nil	Normal	NA	Yes (35/- to 19/-)
	70	c.3325dupC	Duplication	Not reported	De novo	15	M	Japan	Nil	5	Generalized dystonia	RLL	Trunk, neck, BUL, BLL	NA	Yes	Normal	Yes	Nil	Yes	Myoclonus, hypotonia	Normal	NA	Yes (53/- to 36.5/-)
	71	c.5631delG	Deletion	Not reported	De novo	8	M	Japan	Nil	6	Generalized dystonia	LL	Trunk, neck, BUL, BLL	NA	Yes	Normal	Yes	Nil	Yes	Myoclonus	Normal	NA	No
Dai et al., ³ 2019	63	c.1656dupC (p.Lys553 Glnfs*46)	Frameshift	P	Maternal	10	M	China	Positive 2.5	NA	Generalized dystonia	LL, trunk	LL, trunk, larynx, UL, neck and tongue	7	Delayed milestones, moderate to severe ID	Nil	No	Nil	Yes	Nil	Normal	NA	No
	64	c.1656dupC (p.Lys553 Glnfs*46)	Frameshift	P	Maternal	NA	F	China	Positive 42	NA	NA	NA	NA	NA	Delayed milestones, moderate to severe ID	Broad nasal base, bulbous nose tip	No	Nil	Yes	Nil	NA	NA	No
	65	c.1656dupC (p.Lys553 Glnfs*46)	Frameshift	P	Maternal	NA	F	China	Positive 14	NA	NA	NA	NA	NA	Delayed milestones, moderate to severe ID	Broad nasal base, bulbous nose tip	No	Nil	Yes	Nil	NA	NA	No
Miyata et al., ⁴ 2020	66	c.4949C>T (p.Thr1650Met)	Missense	LP	De novo	7	M	Japan	Nil	5	Generalized dystonia	RUL	BUL, BLL	NA	Normal	Thick upper eyelid, broad nasal base, and bulbous nasal tip	No	Nil	No	Asterix at onset	Normal	LEV, CLO	Yes (impr oved)
Cao et al., ⁵ 2019	61	c.4847C > T (p.Ala161 GVal)	Missense	P	De novo	8	M	China	Nil	7	Generalized dystonia	Larynx	RUL, trunk, LL	1	Normal	Elongated facies, bulbous nasal tip	No	Nil	No	Nil	Normal	LD, CLO, CBZ	Yes (73.5/- to 3/-)
Horisawa et al., ⁶ 2020	21	c.5631delG (p.G1879Valfs*15)	Frameshift	Not reported	De novo	19	M	Japan	Nil	6	Generalized dystonia	RLL	Larynx, neck, trunk, all limbs (right predominant)	9	Delay	Normal	Yes	Nil	Yes	Mild cognitive impairment, myoclonic jerks in UL	Normal	Anticholinergics, BOT, RFA (left pallidotomy, a right pallido thalamic tractotomy)	Yes (66/- to 10.5/-)
	22	c.C2275T (p.Gln759*)	Nonsense	Not reported	De novo	34	M	Japan	Nil	10	Generalized dystonia	BUL	Larynx, neck, UL, trunk (left predominant)	22	Delay	Normal	Yes	Nil	Yes	Mild cognitive impairment, myoclonic jerks in UL	Normal	Anticholinergics, CLO, BOT, RFA (right pallido thalamic tractotomy)	Yes (32/- to 21/-)
	23	c.2422_24 23insCAG (p.Gln720ProGlu)	Inframe insertion	Not reported	De novo	29	M	Japan	Nil	14	Generalized dystonia	RUL	Larynx, neck, RUL, trunk (right predominant)	12	Delay	Normal	Yes	Nil	Yes	Mild cognitive impairment, myoclonic jerks in UL	Normal	Anticholinergics, Yes (20.5/- to 7/-) LD, CLO, BOT, RFA (simultaneous left ventro oral thalamotomy and a left pallido thalamic tractotomy)	
Pandey et al., ⁷ 2020	60	c.455G>A (p.Arg152Gln)	Missense	Not reported	Paternal	23	M	India	Nil	19	Generalized dystonia	LL, trunk	Trunks, LL, UL	NA	Normal	Elongated facies	No	Nil	No	Tremors, sensory tricks	Normal	LD, THP, CLO	No
Mun et al., ⁸ 2020	62	c.515dupC (p.Thr172fs)	Frameshift	P	De novo	28	F	Korea	Nil	27	Generalized dystonia	Neck	Neck, larynx, trunk, BUL, BLL	1	Delayed milestones, born pre-term, ID	Nil	Yes	Nil	Yes	Nil	Normal	LD, BAC, THP, DIA	Yes (30/11 to 9/1)
Li et al., ⁹ 2020	24	c.3007C>T, p.Arg1003Trp	Missense	LP	De novo	11	M	China	Nil	8	Segmental dystonia	LUL	LUL, RUL, pharynx	NA	Normal	Broad nasal bridge, bulbous nose tip	No	Nil	Yes	NA	Normal	LD, CLO, BAC, THP	No
	25	c.7373-1G>A, unknown	NA	P	De novo	11	F	China	Nil	9	Generalized dystonia	BLL	BLL, neck, trunk, pharynx	NA	Normal	Broad nasal bridge	No	Nil	No	NA	Normal	LD, CLO, BAC, THP	No
	26	c.1471_14 72insGCAC, p.Ser493 Hisfs*58	Frameshift	P	De novo	72	M	China	Nil	8	Generalized dystonia	RUL	RUL, BLL, trunk, neck, larynx and pharynx	NA	Normal	Broad nasal bridge, bulbous nose tip	No	Nil	NA	Normal	LD, CLO, BAC, THP	Yes (37/- to 15/-)	
	27	c.3060_30 63insGGA, p.Arg102 1Glnfs*3	Frameshift	P	De novo	8	F	China	Nil	6	Generalized dystonia	RLL	BLL, RUL, trunk, larynx	NA	Normal	Normal	No	Nil	No	Advanced bone age	Normal	LD, CLO, BAC, THP	Yes (41/- to 12/-)
	28	c.3140dupG, p.Ala1049 Glyfs*39	Frameshift	P	De novo	16	F	China	Nil	6	Generalized dystonia	BLL	BLL, BUL, trunk, neck	NA	Normal	Broad nasal bridge, bulbous nose tip	No	Nil	No	NA	Normal	LD, CLO, BAC, THP	No
	29	c.3605dupT, p.Met120 2Ilefs*22	Frameshift	P	De novo	11	F	China	Nil	5	Generalized dystonia	RLL	BLL, BUL, trunk, larynx	NA	Normal	Normal	No	Nil	No	Early menstruation and breast development, advanced bone age	Normal	LD, CLO, BAC, THP	No
	30	c.4214dupT, p.Ser1406 Glufs*272	Frameshift	LP	Maternal	16	F	China	Nil	2	Generalized dystonia	Larynx	BLL, RUL, trunk, larynx, pharynx and neck	NA	Mild ID	Normal	Yes	Nil	Yes	Early menstruation	Normal	LD, CLO, BAC, THP	Yes (29/- to 22/-)
	31	c.5462dupC (p.Leu188 2Thrfs*12)/ c.5462dupC (p.Leu188 2Thrfs*12)	Frameshift	LP	Paternal	5	M	China	Nil	2	Generalized dystonia	BLL	BLL, RUL, and trunk	NA	Normal	Elongated facies	Yes	Nil	Yes	NA	Normal	LD, CLO, BAC, THP	Yes (19 to 3)
	32	c.5462dupC, p.Leu188 2Thrfs*12/ c.5462dupC, p.Leu188 2Thrfs*12	Frameshift	LP	Unknown	32	M	China	Nil	7	Generalized dystonia	BLL	BLL, RUL, trunk, and larynx	NA	Normal	Normal	No	Nil	Yes	NA	Normal	LD, CLO, BAC, THP	Yes (12 to 4)
	33	c.5877_58 78insC, p.Gly196 2Trpfs*10	Frameshift	LP	Paternal	8	M	China	Nil	6	Generalized dystonia	BLL	BLL, RUL, trunk, and larynx	NA	Normal	Broad nasal bridge, bulbous nose tip	No	Nil	No	NA	Normal	LD, CLO, BAC, THP	No
	34	c.6408dupC, p.Ala2139 Glyfs*6	Frameshift	P	De novo	20	F	China	Nil	12	Generalized dystonia	BLL	BLL, BUL, and trunk	NA	Normal	Micrognathia, prognathism	Yes	Nil	Yes	NA	Normal	LD, CLO, BAC, THP	No
	35	c.6866delC, p.Pro2289 Argfs*36	Frameshift	P	De novo	7	M	China	Nil	3	Generalized dystonia	LLL	BLL, BUL, trunk, neck, eyes, mouth, and larynx	NA	Normal	Elongated facies, micrognathia	Yes	Nil	Yes	NA	Normal	LD, CLO, BAC, THP	Subjective improvement
	36	c.6890delC, p.Arg229 9Glyfs*26	Frameshift	P	De novo	3	M	China	Nil	1 month	Generalized dystonia	Larynx	BLL, larynx, pharynx and mouth	NA	ID	Normal	No	Nil	No	Advanced bone age	Normal	LD, CLO, BAC, THP	No
Aksoy et al., ¹⁰ 2022	11	c.2453dupT (p.Met818 fs*28)	Frameshift	Not reported	De novo	8	M	Turkey	Nil	8.5	Multifocal dystonia	LUL	Neck, larynx, RLL, LUL	NA	Feeding difficulty, developmental delay	Elongated facies, bulbous nasal tip	Yes	Nil	Yes	Hemichorea, waddling gait, diurnal fluctuation, myoclonus	Normal	LD, THP	No
Kwong et al., ¹¹ 2021	16	c.2425C>T, p.(Gln809*)	Nonsense	P	De novo	29	M	China	Nil	6	Generalized dystonia	NA	NA	NA	Normal	Nil	No	Nil	No	Spasticity, fatty liver, recurrent patellar dislocation, prominent capillaries	Normal	CLO, CBZ, THP, GAB	Yes
Rajan et al., ¹² 2021	17	c.4675G>T (p.Asp1559Tyr)	Missense	VUS	Maternal	17	F	India	Positive 9	NA	Generalized dystonia	LUL and LLL	Lower face, neck, lingual, all limbs	6	Normal	Bulbous nose tip	No	Nil	No	Nil	Normal	LD, TET, CLO	Yes (94/24 to 57.5/22)
Grosz et al., ¹³ 2022	1	c.5073C>T (p.Gly1691=)	Synonymous splice-site variant	P	De novo	22	M	Bangladesh	Nil	9 to 10	Multifocal dystonia	UL and speech	BUL, neck, LL	NA	Normal	Nil	No	Nil	No	Nil	Normal	GAB, LD	No
Wu et al., ¹⁴ 2022	6	c.3043C>T, p.Arg1015*	Nonsense	P	De novo	NA	M	Taiwan	Nil	2	Generalized dystonia	Neck	Neck, trunk, and BUL	2	Normal	Nil	No	Nil	No	Nil	Normal	NA	NA
Shimazaki et al., ¹⁵ 2022	10	c.5285 G>A (p.Arg176 2His)	Missense	P	Not reported	27	F	Japan	Nil	26	Generalized dystonia with tremors	Neck	Neck, striatal toes	1	Mild ID	Elongated facies, bulbous nasal tip	No	Anxiety	Yes	Tremors at RUL and neck	Normal	LD, CLO, BOT	No
Padmanabha et al., ¹⁶ 2021	20	chr19:3622 1280G>A (p.Glu170 5Arg)	Missense	P	De novo	13	M	India	Nil	8	Generalized dystonia	LLL	LUL, orofacial, neck, trunk	NA	Normal	Elongated facies, bulbous nose tip, bushy eyebrows	No	Nil	No	Grey hairs, acne vulgaris, blue-dot cataract, and mid-thoracic scoliosis	Normal	THP, TET, LD, BAC	No
Current study	72	g.36228077A>G	Missense	LP	Unknown	12	M	India	Nil	2	Generalized dystonia	RLL	BLL, UL, neck, trunk, OBL, larynx and biep haro spasm	2	No	Thick lips, coarse facial features, chalky white dentition	No	No	No	Kypho-scoliosis, chalky white dentition	BLGP hypoint ensity	THP, CLO, BAC, LD	No
	73	g.36221499T>C	Missense	LP	Unknown	18	M	India	Nil	13	Generalized dystonia	OM	OM, lingual, jaw opening dystonia, blepharospasm, larynx, bilateral UL, LL, and trunk	1	Yes	Evertedears, higharched palate	No	Yes	No	Genu varum, hammer toes, impaired vertical gaze	BLGP hypoint ensity	THP, TET, CLO, LD, BOT, QUE, VAL, ARI	No
	74	g.36210725delC	Deletion	LP	Unknown	43	F	India	Nil	43	Generalized dystonia	Neck	Lower face, larynx, neck, distalarm, trunk, and LL	3	No	Normal	No	No	No	No	n-specific	BAC, TET, CLO	No
	75	g.36214765delC	Deletion	P	De novo	16	M	India	Nil	5	Generalized dystonia	RLL	Neck, lower face, jaw, trunk, BUL (Pr > Di), and BLL (Pr > Di)	3	No	Normal	Yes	No	Yes	Choreiform movements	BLGP hypoint ensity	THP, TET, CLO, BAC, PRA, LD	No
	76	g.36227689A>G	Missense	LP	Unknown	19	F	India	Nil	19	Generalized dystonia	LL	OM, larynx, lingual, neck, trunk, BUL and BLL	2 months	Yes	Elongated facies, higharched palate	Yes	No	No	Genu valgum in LLL and Genu varum in RLL	Normal	TET, DIA, BAC, CLO, THP	No
	77	g.36223433G>A	Missense	VUS-LP	Unknown	20	M	India	Nil	20	Generalized dystonia	LL	Neck, trunk, UL, and LL	6 months	Yes	Dolicocephaly	No	Yes	No	Normal	Normal	BAC, CLO, THP, PRA, QUE, BOT	No
	78	g.36218074T>A	Missense	LP	Paternal	13	F	India	Nil	9	Generalized dystonia	LLL	Neck, trunk, BUL, tongue mild, BLL	2	No	No	Yes	No	No	Normal	Normal	THP, TET, CLO, LD	No

AAO, age at onset; MRI, magnetic resonance imaging; BAC, baclofen; BFMDRS-M/D, Burke-Fahn-Marsden Dystonia Rating Scale Motor and Disability Scores; BOT, botulinum toxin; BLL, bilateral lower limb; BUL, bilateral upper limb; CLO, clonazepam; DBS, deep brain stimulation; DIA, diazepam; GAB, gabapentin; ID, intellectual disability; LD, levodopa; LL, lower limb; LUL, left upper limb; LP, likely pathogenic; NA, not available; OM, oro-mandibular; OBL, oro-bucco-lingual; P, pathogenic; PRA, pramipexole; RFA, radio-frequency ablation; RLL, right lower limb; RUL, right upper limb; TET, tetrabenazine; THP, trihexyphenidyl; UL, upper limb; F, female; M, male; LEV, levetiracetam; VUS, variant of uncertain significance; LLL, Left lower limb; CBZ, carbamazepine; BLGP, bilateral globus pallidi; QUE, quetiapine; VAL, valproate; ARI, arripiprazole; Pr, proximal; Di, distal.