

Supplementary Table 4. Literature review of all published cases of *KMT2B* related dystonia and neurodevelopmental disorder post Cif et al.²⁵ 2020

Study	Case	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	Developmental abnormality or systemic findings/aID	Facial dysmorphism	Microcephaly	Psychiatric symptoms	Short stature	Additional features	Brain MRI	Medical management	DBS (Yes/No) (BFMDRS-M/D pre and post-DBS)	
Grosz et al., ¹⁷ 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	GBP, LD	No	
Buzo et al., ¹⁷ 2022	2	c.5897C>T (p.Ser1966Phe)	Missense	VUS	De novo	56	F	Spain	Positive (sibling)	52	Cervical dystonia	Neck	Neck, and OM	NA	Normal	Nil	No	OCD, mood disorder	No	Facial tics, OCD, mood disorder	Normal	DUL, TET, MIR, LOR, TOP	Yes (32/14 to 1.5/5)	
	3	c.5897C>T (p.Ser1966Phe)	Missense	VUS	De novo	38	M	Spain	Positive (sibling)	36	Cervical dystonia	Neck	Neck	NA	Normal	Nil	No	OCD	No	Nil	Normal	TET, DIA	Yes (14/10 to 7.5/4)	
Feuerstein et al., ⁴ 2021	4	c.974_979del, p.Ser325Ter	Deletion	Not reported	De novo	33	M	USA	Positive grand father dystonia and parkinsonism	3	Generalized dystonia	Rt foot	RUL, neck, trunk	17	Delayed language milestones	Dysmorphic features (broad nasal bridge, elongated face, low-set ears)	No	Nil	No	Parkinsonism with FOG	Normal	THP, LORA, LD, ROT	Yes (UPDRS 48 to 36)	
Damsio et al., ¹⁹ 2021	5	c.3334+1G>A (p.(Gly 1020_ Asn1 111del)	Inframe deletion	P	De novo	30	F	Portugal	Nil	22	Cerebellar ataxia	Gait	Gait, scanning dysarthria	NA	Normal	Elongated	No	Depression	No	Cerebellar ataxia, cervical dystonia	Normal at 15 years; Cerebellar atrophy; Vermian, superior sulci at 30 years	NA	NA	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	
Owczarzak et al., ²⁰ 2022	7	c.5047C>T (p.Gln1683*)	Nonsense	P	Maternal	10	M	USA	Positive, ID	10	Multifocal dystonia	Larynx	Larynx, LUL, LLL	NA	Mild delay	Down-slanted palpebral fissures, right nasal deviation, elongated chin, retrognathia, asymmetry of lower back	No	Nil	No	Slow saccades, LL spasticity, stooped posture, short stature	Normal	LD, BAC, BOT	No	
	8	c.5047C>T (p.Gln1683*)	Nonsense	P	Maternal	NA	F	USA	Positive, ID	NA	IDD with subtle dystonia	NA	NA	NA	NA	NA	No	ADHD	Yes	Short stature	NA	NA	No	
	9	c.5047C>T (p.Gln1683*)	Nonsense	P	Maternal	NA	F	USA	Positive, ID	NA	Learning disabilities	NA	NA	NA	NA	NA	No	Nil	Yes	Short stature	NA	NA	No	
Shimazaki et al., ¹⁰ 2022	10	c.5285G>A (p.Arg1762His)	Missense	P	Not reported	27	F	Japan	Nil	26	Generalized dystonia with tremors	NA	Neck, striatal toes,	1	Mild ID	Elongated facies, bulbous nasal tip	No	Anxiety	Yes	Tremors at onset involving RUL and neck	Normal	LD, CLO, BOT	No	
Aksoy et al., ¹⁰ 2022	11	c.2453dupT (p.Met918fs*28)	Frameshift	Not reported	De novo	8	M	Turkey	Nil	9	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	
Ng et al., ²¹ 2020	12	c.4960T>C (p.Cys1654Arg)	Missense	P	Maternal	15	F	USA	Positive	3	Generalized dystonia	LLL	Neck, larynx, lingual, OM, RUL, LLL, left foot inversion	11	Mild cognitive impairment	11	No	Nil	No	Contracture left foot	Symmetric hypointensities in BLGP	LD, THP	No	
	13	c.4960T>C (p.Cys1654Arg)	Missense	P	Maternal	34	F	USA	Positive	29	Segmental dystonia	BUL	RUL	NA	Normal	Nil	No	Nil	Nil	Left MCA infarct	NA	NA	No	
	14	c.4960T>C (p.Cys1654Arg)	Missense	P	Maternal	4	M	USA	Positive	NA	Failure to thrive	NA	NA	NA	Delayed milestones	Nil	No	Nil	Yes	Toe walking, hypernasal speech	NA	NA	NA	
	15	c.4960T>C (p.Cys1654Arg)	Missense	P	Maternal	6	F	USA	Positive	NA	Failure to thrive with focal dystonia	NA	NA	NA	Delayed milestones	Nil	No	Nil	Yes	Ceft palate, swallowing difficulty, toe walking, ocular abnormalities; Left strabismus with amblyopia, astigmatism	NA	NA	NA	
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	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)	
Winslow et al., ²² 2020	18	c.4960T>C (p.Cys1654Arg)	Missense	P	Maternal	41	M	USA	Positive	Late 20s	Generalized dystonia	Neck	Neck, all limbs	ID	Nil	Nil	No	Nil	No	Onset with tremors, head bobbing	Normal	Anticholinergics, BOT	Yes (35/4 to 4/1)	
	19	c.4960T>C (p.Cys1654Arg)	Missense	P	Maternal	NA	NA	USA	Positive	NA	Focal dystonia	NA	RUL	NA	Normal	Nil	No	Nil	No	Postural tremors	Normal	NA	No	
Padmanabha et al., ¹⁸ 2021	20	chr19: 36221280 G>A (p.Glu1705Arg)	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	
Horisawa et al., ²⁰ 2021	21	c.5631delG (p.Gly1879Valfs*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 pallidotomy)	Yes (66/- to 10.5/-)	
	22	c.C.2275T (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 pallidotomy)	Yes (32/- to 21/-)	
	23	c.2422_2423insCAG (p.Gln981ProGlu)	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, LD, CLO, BOT, RFA (simultaneous left ventrooral thalamotomy and a left pallidotomy)	Yes (20.5/- to 7/-)	
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_1472insGCAC, p.Ser493Hisfs*58	Frameshift	P	De novo	37	M	China	Nil	8	Generalized dystonia	RUL	RUL, BLL, trunk, neck, larynx and pharynx	NA	Normal	Broad nasal bridge, bulbous nose tip	No	Nil	No	NA	Normal	LD, CLO, BAC, THP	Yes (37/- to 15/-)	
	27	c.3060_3063insGGA, p.Arg1021Glnfs*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.Ala1049Glyfs*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.Met1202Ilefs*22	Frameshift	P	De novo	11	F	China	Nil	5	Generalized dystonia	RLL	BLL, BUL, trunk, larynx	NA	Normal	Normal	No	Nil	No	Earlier menstruation and breast development, advanced bone age	Normal	LD, CLO, BAC, THP	No	
	30	c.4214dupT, p.Ser1406Glnfs*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.Leu1882Thrfs*12), c.5462dupC (p.Leu1882Thrfs*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.Leu1882Thrfs*12, c.5462dupC, p.Leu1882Thrfs*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_5878insC, p.Gly1962Trpfs*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.Ala2139Glyfs*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.6860delC (p.Pro2289Argfs*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.Arg2299Glyfs*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	
Ciolfi et al., ²³ 2021	37	c.649dupC (p.Arg217ProfsTer35)	Frameshift	P	De novo	11	F	Canada	Nil	5	Generalized dystonia	LL, Larynx	BUL, BLL (L > R), OM, neck, and larynx	NA	Language delay, borderline ID	Nil	No	Nil	No	Preocious puberty	Normal	THP, TET, DIA	No	
	38	c.1664dupC (p.Val557GlyfsTer42)	Frameshift	P	De novo	12	M	Canada	Nil	8	Generalized dystonia	LL	BUL (R > L), BLL (R > L), OM, neck, and larynx	NA	Intrauterine growth retardation	Hypertelorism	No	Nil	Yes	NA	Normal	LD, THP	No	
	39	c.3232C>T (p.Arg1078Cys)	Missense	VUS	Undetermined	72	F	Canada	Positive (Father PD)	69	Segmental dystonia	BS	BS, neck	NA	Normal	Elongated	No	Nil	Yes	NA	Normal	BOT	No	
Schreiber et al., ²⁴ 2022	40	c.5392G>A (p.Ala1798Thr)	Missense	VUS	Unknown	69	F	Canada	Nil	63	Focal dystonia	RUL	RUL	NA	Normal	Nil	No	Nil	Yes	NA	Normal	BOT	No	
	41	c.2258_2279dupACAG CCACAGCT (p.Gln759_Pro762dup)	Duplication	VUS	Maternal	11	F	Canada	Nil	< 6 months	Generalized dystonia	NA	BUL, BLL, neck	NA	Motor delay	Nil	No	Nil	No	NA	Normal	NA	NA	
	42	c.1942C>T (p.Arg648Trp)	Missense	VUS	De novo	4	M	Canada	Nil	Birth	Global developmental delay	NA	NA	NA	Delayed milestones	Hypertelorism, deep nasal root, turriophaly	Aggressive behavior	No	Nil	Drooling, jerky movements, LL hypertonia, stereotypies, cryptorchidism and single transverse palmar crease	Normal	NA	No	NA
	43	c.7595G>A (p.Arg2532Gln)	Missense	VUS	De novo	5	M	Canada	Nil	Birth	Developmental delay with moebius syndrome	NA	NA	NA	Delayed milestones, intrauterine growth retardation, club foot	Moebius syndrome	No	Nil	Yes	NA	CC agenesis, VI, VII, and XII agenesis	NA	NA	No
Mirza-Schreiber et al., ²⁴ 2022	44	c.3632G>A (p.Gly1211Glu)	Missense	LP	De novo	NA	NA	Europe	NA	13	Isolated	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	45	c.8566delC (p.Pro2289Argfs*36)	Frameshift	P	Unknown	NA	NA	Europe	NA	6	Isolated	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	46	c.6406delC (p.Leu2136Serfs*17)	Frameshift	P	De novo	NA	NA	Europe	NA	7	Isolated	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	47	c.3700G>A (p.Glu1234Lys)	Missense	LP	De novo	NA	NA	Europe	NA	17	Isolated	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	48	c.7050-2A>G (p.Phe2321Serfs*93)	Frameshift	P	De novo	NA	NA	Europe	NA	11	Complex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	49	c.1633C>T (p.Arg545*)	Nonsense	P	De novo	NA	NA	Europe	NA	3	Complex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	50	c.2428C>T (p.Gln 810*)	Nonsense	P	Paternal	NA	NA	Europe	NA	4	Complex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	51	c.424C>T (p.Arg142*)	Nonsense	P	Unknown	NA	NA	Europe	NA	2	Complex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	52	c.5210dupC (p.Trp176Aspfs*5)	Frameshift	P	De novo	NA	NA	Europe	NA	7	Complex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	53	c.17_23dup (p.Ser9Argfs*109)	Frameshift	P	De novo	NA	NA	Europe	NA	5	Complex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No	
	54	c.4549C>T (p.Arg1517*)	Nonsense	P	De novo	NA	NA	Europe	NA	3	Complex													