Title: Childhood Ataxia with Central Nervous System Hypomyelination/Vanishing White Matter *GeneReview* Table 3
Authors: Schiffmann R, Fogli A, Van der Knaap MS, Boespflug-Tanguy O
Updated: July 2007
Note: The following information is provided by the authors and has not been reviewed by *GeneReviews* staff.

Table 3. Pathologic Allelic Variants

Gene	Exon/Intron	Mutation	Allelic Percentage	Protein Mutation
EIF2B1	Intron 2	IVS2+1G>A	<1%	S84ins22aa, stop
	Exon 6	A622T	<1%	N208Y
	Exon 7	A622T		N208Y
EIF2B2	Exon 4	C512T	<1%	S171F
	Exon 4	C547T	<1%	R183fs
	Exon 4	548Gdel	<1%	R183fs
	Exon 4	C586T		P196S
	Exon 5	G599T	<1%	G200V
	Exon 5	G599C	<1%	G200A
	Exon 5	607-612delins TG	<1%	M203fs
	Exon 5	A638G	8.2%	E213G
	Exon 6	A818G	<1%	K273R
	Exon 7	C871T		P291S
	Exon 8	G910T	<1%	E304X
	Exon 8	T947A	<1%	V316D
	Exon 8	G986T	<1%	G329V
EIF2B3	Exon 1	G136A	<1%	V46I
	Exon 2	C260T	<1%	A87V
	Exon 3	A407C	<1%	Q136P
	Exon 6	G674A	<1%	R225W
	Exon 8	T4023G	<1%	H341Q
	Exon 9	11931195delTG	<1%	V398fs
EIF2B4	Exon 7	C683T	<1%	A228V
	Exon 7	G626A	1.5%	R209Q
	Exon 7	C625T	<1%	R209X
	Exon 8	C728T	3%	P243L
	Exon 9	T806G		L269R
	Exon 11	C1069T		R357W
	Exon 11	G1070A		R357Q

Gene	Exon/Intron	Mutation	Allelic Percentage	Protein Mutation
	Exon 11	G1091T		R364Q
	Exon 11	C1120T	1.1%	R374C
	Exon 11	C1172A	<1%	A391D
	Intron 11	IVS11+1G>A	<1%	E397ins11aa
	Exon 13	T1393C	<1%	C465R
	Exon 13	C1447T	<1%	R483W
	Exon 13	T1465C	1.1%	Y489H
EIF2B5	Exon 1	C47A	<1%	A16D
	Exon 1	G161C	<1%	R54P
	Exon 1	T166G	<1%	F56V
	Exon 2	T203C		L68S
	Exon 2	T218G	1.5%	V73G
	Exon 2	G220A		A74T
	Exon 2	G241A	<1%	E81K
	Exon 2	A271G	7.1%	T91A
	Exon 2	A318T	<1%	L106F
	Exon 3	G338A	27.4%	R113H
	Exon 3	C337T	<1%	R113C
	Exon 3	C406T	<1%	R136C
	Exon 3	453-454del		Y152fsX12
	Exon 4	C545T	<1%	T182M
	Exon 4	G584A	2.2%	R195H
	Exon 4	C583T	<1%	R195C
	Exon 4	G592A	<1%	E198K
	Exon 6	792delTinsACA	<1%	F264fs
	Exon 6	G806T	<1%	R269L
	Exon 6	C805G		R269G
	Exon 6	G806A		R269Q
	Exon 7	G896A	<1%	R299H
	Exon 7	G925C	1.5%	V309L
	Exon 7	G929T		C310F
	Exon 7	C943G	<1%	R315G
	Exon 7	G944A	<1%	R315H
	Exon 7	C943T	<1%	R315C
	Exon 7	C967T	<1%	P323S

Gene	Exon/Intron	Mutation	Allelic Percentage	Protein Mutation
	Exon 7	T1003C		C335R
	Exon 7	C1015T	3.4%	R339W
	Exon 7	G1016C	<1%	R339P
	Exon 7	G1016A	<1%	R339Q
	Exon 7	G1016T		R339P
	Exon 7	A1028G	<1%	Y343C
	Exon 7	A1153G	<1%	I385V
	Exon 8	G1157T	<1%	G386V
	Exon 8	A1160G	<1%	D387G
	Exon 8	C1264T	<1%	R422X
	Exon 8	T1274G	<1%	L425R
	Exon 8	C1280T	<1%	P427L
	Exon 8	T1289C	<1%	V430A
	Exon 9	C1340T	<1%	S447L
	Exon 9	G1444ins17	<1%	G481fs493X
	Exon 9	G1459A		E487K
	Exon 10	A1484G	<1%	Y495C
	Exon 13	1813delC		L605fs
	Exon 14	T1882C	<1%	W628R
	Exon 14	G1884A	<1%	W628X
	Exon 14	G1948A	1.2%	E650K
	Exon 14	1996del21	<1%	664del7

www.vumc.nl/whitematter

Mutations can affect all regions of the five eIF2B subunits. From Leegwater et al [2001], van der Knaap et al [2002], van der Knaap et al [2003], Fogli et al [2004b], Ohtake et al [2004], Ohlenbusch et al [2005], Fogli & Boespflug-Tanguy [2006], Pronk et al [2006], Scali et al [2006], Matsui et al [2007].

References

Fogli A, Boespflug-Tanguy O. The large spectrum of eIF2B-related diseases. Biochem Soc Trans. 2006;34:22-9.

Fogli A, Schiffmann R, Hugendubler L, Combes P, Bertini E, Rodriguez D, Kimball SR, Boespflug-Tanguy O. Decreased guanine nucleotide exchange factor activity in eIF2B-mutated patients. Eur J Hum Genet. 2004b;12:561-6.

Leegwater PA, Vermeulen G, Konst AA, Naidu S, Mulders J, Visser A, Kersbergen P, Mobach D, Fonds D, van Berkel CG, Lemmers RJ, Frants RR, Oudejans CB, Schutgens RB, Pronk JC, van

der Knaap MS. Subunits of the translation initiation factor eIF2B are mutant in leukoencephalopathy with vanishing white matter. Nat Genet. 2001;29:383-8.

Matsui M, Mizutani K, Ohtake H, Miki Y, Ishizu K, Fukuyama H, Shimohata T, Onodera O, Nishizawa M, Takayama Y, Shibasaki H. Novel mutation in EIF2B gene in a case of adult-onset leukoencephalopathy with vanishing white matter. Eur Neurol. 2007;57:57–8

Ohlenbusch A, Henneke M, Brockmann K, Goerg M, Hanefeld F, Kohlschütter A, Gärtner J. Identification of ten novel mutations in patients with eIF2B-related disorders. Hum Mutat. 2005;25:411

Ohtake H, Shimohata T, Terajima K, Kimura T, Jo R, Kaseda R, Iizuka O, Takano M, Akaiwa Y, Goto H, Kobayashi H, Sugai T, Muratake T, Hosoki T, Shioiri T, Okamoto K, Onodera O, Tanaka K, Someya T, Nakada T, Tsuji S. Adult-onset leukoencephalopathy with vanishing white matter with a missense mutation in EIF2B5. Neurology. 2004;62:1601-3.

Pronk JC, van Kollenburg B, Scheper GC, van der Knaap MS. Vanishing white matter disease: a review with focus on its genetics. Ment Retard Dev Disabil Res Rev. 2006;12:123-8.

Scali O, Di Perri C, Federico A. The spectrum of mutations for the diagnosis of vanishing white matter disease. Neurol Sci. 2006;27:271-7.

van der Knaap MS, Leegwater PA, Konst AA, Visser A, Naidu S, Oudejans CB, Schutgens RB, Pronk JC. Mutations in each of the five subunits of translation initiation factor eIF2B can cause leukoencephalopathy with vanishing white matter. Ann Neurol. 2002;51:264-70.

van der Knaap MS, van Berkel CG, Herms J, van Coster R, Baethmann M, Naidu S, Boltshauser E, Willemsen MA, Plecko B, Hoffmann GF, Proud CG, Scheper GC, Pronk JC. eIF2B-related disorders: antenatal onset and involvement of multiple organs. Am J Hum Genet. 2003;73:1199-207.