Title: *ATP1A3*-Related Neurologic Disorders *GeneReview* Table 2
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Note: The following information is provided by the authors and has not been reviewed by *GeneReviews* staff.

Table 2. *ATP1A3* Genotypes as They Correlate with RDP, AHC, and CAPOS Phenotypes

Nucleotide Change	Protein Change	Phenotype	Inherited or *de novo* Mutation	Recurrent (Yes/No), Frequency
410C>A	Ser137Tyr	AHC	*de novo*	Yes, infrequent
410C>T	Ser137Phe	AHC	*de novo*	No
419A>T	Gln140Leu	AHC	*de novo*	No
821T>A	Ile274Asn	AHC	*de novo* Familial (dominant)	Yes, infrequent
821T>C	Ile274Thr	RDP	*de novo*	No
829G>A	Glu277Lys	RDP	*de novo*	Yes, infrequent
965T>A	Val322Asp	AHC	*de novo*	Yes, infrequent
979_981delCTG	Leu327del	RDP	*de novo*	No
998G>T	Cys333Phe	AHC	*de novo*	Yes, infrequent
1003A>C	Thr335Pro	AHC	*de novo*	No
1072G>T	Gly358Cys	AHC	*de novo*	No
1109C>A	Thr370Asn	RDP	*de novo*	No
1112T>C	Leu371Pro	AHC	*de novo*	No
1144T>C	Trp382Arg	RDP	*de novo*	No
1250T>C	Leu417Pro	RDP	*de novo*	No
1838C>T	Thr613Met	RDP	*de novo* Familial (dominant)	Yes, intermediate N = 6
2051C>T	Ser684Phe	RDP	*de novo*	No
2264G>C	Gly755Ala	AHC	*de novo*	No
2263G>A	Gly755Ser	AHC	*de novo*	Yes, infrequent
2263G>T	Gly755Cys	AHC	*de novo*	Yes, infrequent
2267G>A	Arg756His	RDP	*de novo*	No
2270T>C	Leu757Pro	AHC	*de novo*	No
2273T>G	Ile758Ser	RDP	Familial (dominant)	No
2312C>A	Thr771Asn	AHC	*de novo*	No
2316C>A	Ser772Arg	AHC	*de novo*	No
2318A>G	Asn773Ser	AHC	*de novo*	No
2318A>T	Asn773Ile	AHC	*de novo*	No
2338T>C	Phe780Leu	RDP	Familial (dominant)	No
Not reported	Asp801Glu	AHC	*de novo* /familial	No (twins)
2401G>A	Asp801Asn	AHC	*de novo*	Yes, frequent N >60 reported

Nucleotide Change	Protein Change	Phenotype	Inherited or *de novo* Mutation	Recurrent (Yes/No), Frequency
2401G>T	Asp801Tyr	RDP	Familial	No
2411C>T	Thr804Ile	AHC	*de novo*	Yes, infrequent
2415C>G	Asp805Glu	AHC	*de novo*	No
2417T>G	Met806Arg	AHC	*de novo*	No
2428A>T	Ile810Phe	AHC	*de novo*	No
2429T>G	Ile810Ser	AHC	*de novo*	No
2431T>C	Ser811Pro	AHC	*de novo*	Yes, infrequent
2443G>A	Glu815Lys	AHC	*de novo*	Yes, frequent N >40 reported
2452G>A	Glu818Lys	Capos	*de novo* Familial (dominant)	Yes, low frequency N = 3 families; 1 *de novo*
2542+1G>A	Splice site	AHC	*de novo*	Yes, infrequent
2600G>A	Gly867Asn	RDP/AHC		No
2755_2757delGTC	Val919del	AHC	*de novo*	No
2767G>A	Asp923Asn	AHC/RDP	Familial (AHC) *de novo* & familial (RDP)	Yes, low frequency N = 5
2767G>T	Asp923Thr	AHC	*de novo*	No
2780G>A	Cys927Tyr	AHC	*de novo*	No
2780G>T	Cys927Phe	AHC	*de novo*	Yes, infrequent
2781C>G	Cys927Trp	AHC	*de novo*	No
2839G>A	Gly947Arg	AHC	*de novo*	Yes, intermediate N >10
2839G>C	Gly947Arg	AHC	*de novo*	Yes, low frequency N = 4
2864C>A	Ala955Asp	AHC	*de novo*	No
2974G>T	Asp992Tyr	AHC	*de novo*	Yes, infrequent
3038_3040dupACT	Tyr1013dup	RDP	*de novo*	No

AHC = alternating hemiplegia of childhood

RDP = rapid-onset dystonia parkinsonism

CAPOS = cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss

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Reference Sequences: NM_152296.3; NP_689509.1

RDP. Fourteen variants have been described to date to cause RDP (reviewed in Heinzen et al 2014, Rosewich et al 2014).

- Three are recurrent:
    - c.829G>A encoding p.Glu277Lys (~13% all de novo) [de Carvalho Aguiar et al 2004, Brashear et al 2007, Tarsy et al 2010];
    - c.1838C>T resulting in p.Thr613Met (~26% both *de novo* and familial occurrence) [de Carvalho Aguiar et al 2004, Brashear et al 2007, Lee et al 2007, McKeon et al 2007; Barbano 2012];
    - c.2767G>A encoding p.Asp923Asn (~8% all *de novo*) [Zanotti-Fregonara et al 2008, Anselm et al 2009].
- The following mutations have been reported at least once: c.821T>C (p.Ile274Thr); c.979_981delCTG (p.Leu327del); c.1109C>A (p.Thr370Asn); c.1144T>C (p.Trp382Arg); c.1250T>C (p.Leu417Pro); c.2051C>T (p.Ser684Phe); c.2267G>A (p.Arg756His); c.2273T>G (p.Ile758Ser); c.2338T>C (p.Phe780Leu); c.2401G>T (p.Asp801Tyr); c.3038_3040dupACT (p.Tyr1013dup).

AHC. More than 30 pathogenic variants have been reported to result in an AHC phenotype in more than 150 individuals.

- The following mutations are recurrent and occur at a reasonably high frequency; together they account for ~ 2/3 of simplex cases reported to date:
    - c.2401G>A in exon17 resulting in p.Asp801Asn (~40%)
    - c.2443G>A in exon 17 resulting in p.Gly815Lys (~24%)
    - c.2839G>A and c.2839G>C in exon 21 resulting in p.Gly947Arg (~8%)
- The following mutations have been reported more than once, but at a much lower frequency: c.410C>A (p.Ser137Tyr); c.821T>A (p.Ile274Asn); c.965T>A (p.Val322Asp); c.998G>T (p.Cys333Phe); c.2263G>A (p.Gly755Ala); c.2263G>A (p.Gly755Ser); c.2263G>T (p.Gly755Cys); c.2411C>T (p.Thr804Ile); c.2431T>C (p.Ser811Pro); splice site change c.2452+1G>A; c.2780G>T (p.Cys927Phe); c.2974G>T (p.Asp992Tyr).
- The following mutations have been reported at least once: c.410C>T (p.Ser137Phe); c.419A>T (p.Gln140Leu); c.1003A>C (p.Thr335Pro); c.1072G>T (p.Gly358Cys); c.1112T>C (p.Leu371Pro); c.2264G>C (p.Gly755Ala); c.2270T>C (p.Leu757Pro; c.2312C>A (p.Thr771Asn); c.2316C>A (p.Ser772Arg); c.2318A>G (p.Asn773Ser); c.2318A>T (p.Asn773Ile); c.2415C>G (p.Asp805Glu); c.2417T>G (p.Met806Arg); c.2428A>T (p.Ile810Phe); c.2429T>G (p.Ile810Ser); c.2600G>A (p.Gly867Asn); c.2755_2757delGTC (p.Val919del); c.2767G>A (p.Asp923Asn); c.2767G>T (p.Asp923Thr); c.2780G>A (p.Cys927Thr); c.2781C>G (p.Cys927Trp); c.2864C>A (p.Ala955Asp).

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