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 Scientific Director: George Nasioulas PhD

SAMPLE INFORMATION

Name :	-	Date Received :	-
Medical ID :	-	Date of Report :	-
Date of Birth :	-	Req. Physician :	-
Location :	-	Barcode :	-
Material :	WHOLE PERIPHERAL BLOOD	Reason of referral:	Spinocerebellar Ataxias (SCA)

CerebrumDX Ataxia analysis

Results associated with the reason of referral

NEGATIVE

The tested sample carries a normal number of (CAG)/(CTA/CTG) repeats for SCA1, SCA2, SCA3, SCA6, SCA7, and SCA8 subtypes.

SCA subtype	Gene	Number of repeats per allele	Number of repeats per allele
SCA1	ATXN1	30 (+/-1)	32 (+/-1)
SCA2	ATXN2	22 (+/-1)	22 (+/-1)
SCA3	ATXN3	20 (+/-1)	23 (+/-1)
SCA6	CANCA1A	12 (+/-1)	13 (+/-1)
SCA7	ATXN7	10 (+/-1)	10 (+/-1)
SCA12	PPP2R2B	10 (+/-1)	15 (+/-1)
SCA17	TBP	38 (+/-1)	38 (+/-1)
DRPLA	ATN1	10 (+/-1)	12 (+/-1)

Methodology

Genomic DNA was extracted from the tested sample. Analysis of CAG and CTA/CTG trinucleotide repeat expansions was performed using the commercially available **Adellgene SCAs kit**. This assay enables the detection and sizing of trinucleotide repeat expansions in genes associated with **SCA1, SCA2, SCA3, SCA6, SCA7, SCA12, SCA17, and DRPLA**.

The methodology is based on polymerase chain reaction (PCR), followed by fluorescent fragment analysis using a genetic analyzer. The size of the resulting PCR products is subsequently converted into the corresponding number of CAG or CTA/CTG repeats.

Note:

As with any molecular genetic assay, an inherent error rate of approximately 0.5–1% may occur due to rare molecular events and technical factors related to sample preparation and analysis.



Electronically Signed by - **Georgia Pepe, MSc Molecular Biologist, AMKA:09038403029**

- **George Nasioulas, PhD Molecular Biologist, Scientific Director, AMKA:26025301255**

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Cerebrum DX *Ataxia*

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This method is validated for the detection of trinucleotide repeat alleles ranging from 5 to 200 repeats.

Sequence variants, including frameshift or missense variants located within primer-binding sites, may interfere with PCR amplification and potentially lead to inaccurate repeat sizing or allele dropout. Results indicating apparent homozygosity should therefore be confirmed using an alternative method.

The accuracy of repeat sizing is ± 1 repeat for alleles containing fewer than 50 repeats and ± 3 repeats for alleles containing 50–200 repeats.

Details about non-pathogenic variants

Autosomal dominant cerebellar ataxias (ADCAs), also referred to as spinocerebellar ataxias (SCAs), comprise a clinically and genetically heterogeneous group of neurogenetic disorders characterized by progressive degeneration of the cerebellum and its connections. This degeneration typically results in gait instability, cerebellar dysarthria, oculomotor abnormalities, and impaired coordination of voluntary movements.

The overall prevalence of autosomal dominant cerebellar ataxias is estimated to be approximately 1–3 per 100,000 individuals in European populations [1,2]. More than 35 distinct SCA subtypes have been described. SCA subtypes have traditionally been numbered sequentially according to the order in which the corresponding genetic loci were identified (e.g., SCA1, SCA2, SCA3) [3,4].

Several of the most common autosomal dominant SCAs are caused by CAG trinucleotide repeat expansions. Among these, SCA3, SCA6, SCA1, SCA2, and SCA7 are among the most frequently reported, although their relative frequencies vary considerably across different populations and geographic regions. In the Greek population, SCA7, SCA1, and SCA2 have been reported among the more frequently observed SCA subtypes [4].



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Genes Analyzed (Table 1)

SCA subtype	Gene	Expansion	Wild type	Uncertain	Reduced Penetrance	Full Penetrance (Mutant)
SCA1	<i>ATXN1</i>	(CAG) _n (CAT) _n (CAG) _n	6-38; 39-44 CAT interrupted	-	-	39-44 CAGs uninterrupted; 45-91
SCA1	<i>ATXN1</i>	(CAG) _n (CAT) _n (CAG) _n	6-35; 39-44 CAT interrupted	36-38	-	39-44 CAGs (Uninterrupted)
SCA2	<i>ATXN2</i>	[(CAG) _n CAA (CAG) _n] (CAG) _n _n	14-31	31-32	33-34	35-500
SCA3	<i>ATXN3</i>	(CAG) 2CAA AAG CAG CAA (CAG) _n	12-44	45-59	-	60-87
SCA6	<i>CACNA1A</i>	(CAG) _n	4-18	19	-	20-33
SCA7	<i>ATXN7</i>	(CAG) _n	7-27	28-33	34-36	36-460
SCA12	<i>PPP2R2B</i>	(CAG) _n	7-31	32-50	-	51-78
SCA17	<i>TBP</i>	[(CAG) _n (CAA) _n] (CAG) _n _n	25-40	-	41-48	49-66
DRPLA	<i>ATN1</i>	(CAG) _n	6-35	-	35-47	48-93



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Literature

1. Sullivan R., Yan Yaul W., O Connor E., Houlden H. **Spinocerebellar ataxia: an update.** Journal of Neurology (2019) 266:533-544. <https://doi.org/10.1007/s00415-018-9076-4> ((PMID: 30284037))
2. Jayadev S., Bird D. T. **Hereditary ataxias: overview.** Genetics in Medicine volume (2013) 15 9, 673-683. ((PMID: 23538602))
3. Mundwiler A., Shakkottai G. V. **Autosomal-dominant cerebellar ataxias.** Handb Clin Neurol (2018);147:173-185. doi: 10.1016/B978-0-444-63233-3.00012-9. ((PMID: 29325610))
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5. Aydin G., Dekomien G., Hoffjan S, Gerding M., W., Epplen T. J., Arning L. (2018) **Frequency of SCA8, SCA10, SCA12, SCA36, FXTAS and C9orf72 repeat expansions in SCA patients negative for the most common SCA subtypes.** BMC Neurology. 2018 Jan 9;18(1):3. doi: 10.1186/s12883-017-1009-9. ((PMID: 29316893))



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