Cerebrum DX *Ataxia*

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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 referal:**	Spinocerebellar Ataxias (SCA)

RP PCR-Fragment analysis

Results

NEGATIVE

The sample under investigation carries a normal number of repeats (CAG)/(CTA/CTG) for the SCA1, SCA2, SCA3, SCA6, SCA7, and SCA8 types of ataxia.

Ataxia	Gene	Number of repeats per allele	Number of repeats per allele
SCA1	*ATXN1*	29 (+/-1)	29 (+/-1)
SCA2	*ATXN2*	22 (+/-1)	22 (+/-1)
SCA3	*ATXN3*	20 (+/-1)	7 (+/-1)
SCA6	*CANCA1A*	12 (+/-1)	12 (+/-1)
SCA7	*ATXN7*	10 (+/-1)	13 (+/-1)
SCA8	*ATXN8*	18 (+/-1)	18 (+/-1)

Methodology

Genomic DNA was extracted from the sample under investigation. The analysis of trinucleotide repeat expansions CAG and CTA/CTG was conducted using the commercially available Adellgene SCAs kit. This particular kit enables the detection of trinucleotide repeats in genes associated with the SCA 1, SCA 2, SCA 3, SCA 6, SCA 7, and SCA 8 subtypes. The methodology is based on polymerase chain reaction (PCR) amplification and size checking of the resulting product using fluorescence analysis on a genetic analyzer. Subsequently, the size of the PCR product is converted into the number of CAG or CTA/CTG repeats.

*Note:
Each molecular analysis has an internal error probability of 0.5-1%. This is due to rare molecular events and factors involved in the preparation and analysis of samples.
This specific methodology detects alleles with trinucleotide expansions < 200. For SCA2, SCA7, and SCA8 subtypes with repeat numbers > 200, an alternative methodology is required.

Electronically Signed by **- Georgia Pepe, MSc Molecular Biologist, AMKA:09038403029**
- George Nasioulas, PhD Molecular Biologist, Scientific Director, AMKA:26025301255

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Frame-shift variants or erroneous primer binding site variations may lead to inaccurate estimation of repeat numbers in alleles. Results in homozygosity require confirmation with an alternative methodology.
The accuracy in determining the repeats is +/- 1 for trinucleotide expansions < 50 and +/-3 between 50-200.

Information about Spinocerebellar Ataxias (SCA)

Autosomal dominant cerebellar ataxias (ADCA), also known as spinocerebellar ataxias (SCA), comprise a heterogeneous group of neurogenetic diseases characterized by degeneration of the cerebellum and its connections. This degeneration leads to gait instability, cerebellar dysarthria, oculomotor disturbances, and movement coordination disorders. ADCA has an overall prevalence of approximately 1-3 per 100,000 in European populations. Over 35 different types of SCA have been described to date. Based on the chronological identification of the genetic locus associated with a specific dominant ataxia, a number is added from 1-37 to the acronym SCA (e.g., SCA1, SCA2, SCA3, etc.). The most common types of ADCA are caused by expansion of a nucleotide triplet (CAG) and are, in descending order, SCA3, SCA6, SCA1, SCA2, and SCA7, although these rates vary significantly from country to country. However, in the Greek population, subtypes SCA7 and SCA1 are more frequently observed. Additionally, the presence of SCA8 expansions has been observed in the Greek population. SCA8 ataxia is caused by an expansion of a combination of nucleotide triplets CTA/CTG located in a non-coding region of the gene.

Genes analyzed (Table 1)

Ataxia	Gene affected	Repeat expansion	Normal range	Uncertain	Reduced Penetrance	Full Penetrance
SCA1	*ATXN1*	(CAG)n (CAT)n (CAG)n	6-38; 39-44 CAT interrupted	-	-	39-44 CAGs uninterrupted; 45-91
SCA2	*ATXN2*	[(CAG)n CAA (CAG)n]n	14-31	32-34	-	35-500
SCA3	*ATXN3*	$(CAG)_2$CAA AAG CAG CAA (CAG)n	11-44	45-59	-	61-87
SCA6	*CACNA1A*	(CAG)n	4-18	-	19	20-33

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SCA7	*ATXN7*	(CAG)n	4-19	28-33	34-35	36-460
SCA8	*ATXN8/ ATXN8OS*	(CTA/CTG)	14-42	-	>=74-1000	-

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Family tree

Note: **The information shown on the family tree has been provided by the patient and not by medical records.**

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Βιβλιογραφία

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))
4. Koutsis G, Kladi A., Karadima G., Houlden H., Wood N.W., Christodoulou C., Panas M. **A study of hereditary ataxias in the Greek population.** Archives of Hellenic Medicine 2014, 31(4):433-445. ((PMID: 24209901))
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))