CeGaT GmbH | Paul-Ehrlich-Str. 23 | D-72076 Tübingen | Germany

Dr. Jane Doe
Paul-Ehrlich-Str. 23
D-72076 Tübingen

Patient	XXX, XX
ID #	Male (*DD.MM.YYYY)
Sample receipt	xxx
Material	EDTA blood
External ID	#
Report date	xxx
Report-ID	R#

Genetic Report – XXX, XX (*DD.MM.YYYY)

Indication Ataxia; lower limb ataxia, dysarthria, dysphagia, neuropathy

Order Repeat analyses: *ATXN1*, *ATXN2*, *ATXN3*, *CACNA1A*, *ATXN7, TBP,* and *FXN*.

Result: Report with Significant Findings

- **Detection of a pathogenic repeat expansion in the gene *ATXN2* (SCA2), which is causative for spinocerebellar ataxia type 2 (SCA2) in your patient.**
- No detection of a pathogenic repeat expansion in the genes *ATXN1* (SCA1), *ATXN3* (SCA3), *CACNA1A* (SCA6), *ATXN7* (SCA7), *TBP* (SCA17), and *FXN* (FRDA).

Gene	Phenotype	OMIM	Heredity	Allele 1	Allele 2	Normal	Intermediate	Pathogenic for
ATXN2	**SCA2**	**#183090**	**AD**	**22±1**	**35±1**	**up to 31 repeats**	**32**	**>32 repeats**

Recommendation

We recommend further clinical management according to the current guidelines for spinocerebellar ataxia type 2 (Pulst, updated 2019, PMID: 20301452, GeneReviews).

Predictive testing of adult asymptomatic family members regarding the repeat expansion identified in gene *ATXN2* may only be performed following genetic counseling.

Genetic Relevance

Your patient is a heterozygous carrier of a pathogenic repeat expansion in the *ATXN2* gene, which has a 50% likelihood of being passed on to future offspring, and may also be relevant for other family members and relatives.

Clinical Information and Variant Interpretation

ATXN2

OMIM / Reference	Phenotype	Heredity
183090	Spinocerebellar ataxia type 2 (SCA2)	AD

The ***ATXN2*** gene encodes the protein ataxin-2, which is ubiquitously expressed, but its function has not yet been fully clarified. The RNA-binding protein presumably plays a role in the regulation of endocytotic processes and gene expression (Nonis et al., 2008, PMID: 18602463; Yokoshi et al., 2014, PMID: 24954906). Following autosomal dominant mode of inheritance, spinocerebellar ataxia type 2 (SCA2) is caused by the expansion of a CAG repeat in *ATXN2* (OMIM # 183090). SCA2 is characterized by cerebellar ataxia, dysarthria, and nystagmus or slow saccadic eye movements, with typical onset in the third or fourth decade (average age of onset: 30 years; age range: 2-65 years).

ATXN2, repeat expansion: 35±1 CAG repeats (het.)

Classification:	Pathogenic

Genetic counseling should be offered with all diagnostic genetic testing, especially following the identification of the molecular cause of a genetic disease.

Medical report written by: XXX

Proofread by: XXX

Validated by: XXX

With kind regards,

Dr. med. Dr. rer. nat. Saskia Biskup

Consultant for Human Genetics

Additional Information

Requested Regions

ATXN1 (SCA1-Repeat), ***ATXN2*** (SCA2-Repeat), ***ATXN3*** (SCA3-Repeat), ***CACNA1A*** (SCA6-Repeat), ***ATXN7*** (SCA7-Repeat), ***TBP*** (SCA17-Repeat), ***FXN*** (FRDA-Repeat)

Methods

Repeat analysis: A repeat spanning polymerase chain reaction (PCR) was performed to determine the copy number of CAG repeats in the corresponding regions of the genes *ATXN1*, *ATXN2*, *ATXN3*, *CACNA1A*, *ATXN7*, and *TBP*. This was followed by separation and sizing of the PCR fragments by capillary electrophoresis.

A repeat spanning polymerase chain reaction (PCR) was performed to determine the copy number of GAA repeats in the first intron of the *FXN* gene. Additionally, a triplet repeat primed PCR (TP-PCR, Ciotti et.al., 2004, PMID: 15507666) was performed to test for very large repeat expansions. This was followed by separation and sizing of the PCR fragments by capillary electrophoresis.

In case of homozygous results, the existence of a large expansion, which cannot be detected by PCR, cannot generally be excluded.

Please be aware that due to the possibility of rare variants in a primer binding site, the unlikely event of an *allelic dropout* cannot be excluded for molecular diagnostics based on PCR technology.

The sample fulfilled our quality criteria upon arrival and during/after each processing step in the laboratory.

The procedure described above was developed and validated in-house (Laboratory developed test; LDT).

Appendix

No known pathogenic repeat expansions were detected in the following analyzed genes, based on current scientific knowledge:

Gene	Phenotype	OMIM	Heredity	Allele 1	Allele 2	Normal	Intermediate	Pathogenic for
ATXN1	SCA1	#164400	AD	31±1	32±1	up to 35 repeats	36-38	>38 repeats
ATXN3	SCA3	#109150	AD	15±1	23±1	up to 44 repeats	45-59	>59 repeats
CACNA1A	SCA6	#183086	AD	11±1	13±1	up to 18 repeats	19	>19 repeats
ATXN7	SCA7	#164500	AD	11±1	11±1	up to 27 repeats	28-36	>36 repeats
TBP	SCA17	#607136	AD	37±1	38±1	up to 40 repeats	41-48	>48 repeats
FXN	FRDA	#229300	AR	17±1	20±1	up to 33 repeats	34-65	>65 repeats

Note: In case of homozygous results, the existence of a large expansion, which cannot be detected by PCR, cannot generally be excluded.

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