MGZ

Medizinisch Genetisches Zentrum

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University Clinic Zurich
Dr. med. Thomas Mann
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GENETIC ASSESSMENT

Munich, 03.03.017djp

Name	Mustermann, Max	**Date of receipt / Start**	01.01.17 / 02.01.17
Date of Birth	30.06.1958	**Sex**	male
ID / your Ref	MGZ 654987 / DN16/1234	**Sample**	EDTA blood
Analysis	*ID286.00*	**Test(s) requested**	*ID 286.00*
Indication	Hereditary Motor and Sensory Neuropathy		

RESULTS

NORMAL RESULT

Panel-ID286.00	Sequencing Deletion/Duplication (analyzed genes, see Appendix)	no pathogenic variant detected no deletion / duplication detected

INTERPRETATION

No pathogenic variant was indentified in the gene panel ID286.01. Thus the clinical diagnosis of Hereditary Motor and Sensory Neuropathy caused by a pathogenic variant in the gene ID286.01 cannot be confirmed.

If, based on clinical symptoms, you would like to consider further genetic studies, we can offer an appropriate single gene analysis or analysis via one of our NGS multi-gene panels (see www.mgz-muenchen.com for available analyses).

METHOD

Next Generation Sequencing to detect mutations in all coding exons as well as their flanking intronic regions using DNA-targeted enrichment (Agilent SureSelectXT or TruSight™ Cancer FC-121-0202, Illumina® sequencing technology). Bioinformatic analysis of collected sequencing data for the detection of SNVs and Indels is performed by means of BWA version 0.7.13-r1126, SAMtools version 1.3.1, snpEff version 4.2 and Alamut-Batch version 1.4.4. (Sensitivity 99.89%, PPV 99.83% with > 30-fold coverage). Detection of deletions/duplications is performed using a modified pipeline based on ExomeDepth 1.1.10, CANOES 2014, CLAMMS 1.0, CODEX 1.5.0 (Sensitivity 80.91%, PPV 95.62% at >30-fold coverage). Reference sequence: GRCh37/hg19 Assembly. For technical reasons, the detection of larger deletions and/or duplications, structural rearrangements, repeat expansions, pathogenic variants in homopolymer regions, in paralogs/pseudogenes and in untested regulatory regions is not possible. Regions with incomplete coverage as defined by our diagnostic criteria are listed in the appendix. Test reports are a product of thorough interpretation of bioinformatic analysis in accordance with the most recent scientific data and take into account all available clinical information provided about a particular patient. The assessment of all identified sequence variants is made by scientists and medical specialists working in close cooperation. We generally report all variants of the classes 4 and 5 (http://www.mgz-muenchen.com/mgz-sequence-variant-classification-system.html). Class 3 variants are reported if the mode of inheritance, allele frequency, bioinformatics prediction and the

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Die Akkreditierung gilt für den in der Urkundenanlage D-ML-13242-01-00 festgelegten Umfang.

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GENETIC ASSESSMENT

Name	Mustermann, Max	**Sample ID**	654987
Date of Birth	30.06.58	**Analysis**	*ID286.01*

given clinical phenotype warrant further evaluation to clarify their possible relevance in the disease. A list of all detected normal variants and class 3 variants which according to current scientific knowledge are not phenotypically relevant can be provided upon request. The nomenclature of sequence variants is in accordance with the HGVS recommendations (den Dunnen JT et al.; Hum Mutat 37:564-569, 2016). Variants are submitted to locus-specific, publically accessible databases.

Should you have any questions or concerns, please do not hesitate to contact us.

Validation
Dr. rer. nat XXXX
XXXXXX
Dr. med. XXXXX *Prof. Dr. med. E. Holinski-Feder / PD Dr. med. A. Abicht*

Certified in accordance with DIN EN ISO 15189:2014. Genetic analyses have a high, however not 100% sensitivity and, as with all laboratory analyses, have an error rate due to pre-analytic, analytic, and post-analytic processes. This test result is based on the scientific data available at the time of reporting. The interpretation of familial test results is only valid provided that the familial relations given are correct. The results of genetic testing should be disclosed within the framework of genetic counseling, especially in cases of a positive result.

Appendix 1: Genes analyzed in the Panel for Sample ID 100010:
Neuropathy, motor and sensory - CMT1 - basis diagnostics ID 286.00

Gene	OMIM	RefSeq
FIG4	609390	NM_014845.5
GDAP1 #	606598	NM_018972.2
GJB1 #	304040	NM_001097642.2
IGHMBP2 #	600502	NM_002180.2
LITAF #	603795	NM_001136473.1
MFN2	608507	NM_014874.3
MPZ #	159440	NM_000530.7
NEFL #	162280	NM_006158.4
PMP22 #	601097	NM_000304.3
SH3TC2	608206	NM_024577.3

In addition to sequence analysis, gene dose analysis to detect genomic deletions / duplications.

Appendix 2: Information on the method and quality of sequencing

The analysis of the multi-gene panel *Neuropathy, motor and sensory - CMT1 - basis diagnostics ID 286.00* fulfilled the NGS diagnostic quality *Type B*.

Coverage with at least 30-fold sequencing depth: **100.00 %**

In order to calculate coverage, all coding exons as well as flanking regions (+/- 5 nucleotides) of the genes listed in Appendix 1 are taken into account.

See additional information under http://www.mgz-muenchen.com/multi-gene-panels.html

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