CeGaT

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Dr. Jane Doe
Paul-Ehrlich-Str. 23
72076 TÜBINGEN
GERMANY

Patient	XXX, XX (*DD.MM.YYYY)
Sex	Male
Patient-ID	#
Sample receipt	xxx
Material	DNA
Report date	xxx

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

Indication	Recurrent febrile convulsions, dysplastic stigmata: thin lips, small nose; speech / language impairment; normal EEG, no skin abnormalities
Order	**1. Array-CGH** 2. Panel Diagnostics (pending)

Dear Dr. Doe,

Thank you for your request for molecular genetic analysis.

RESULTS

- **Array CGH analysis revealed a hemizygous deletion of approx. 1.6 Mb on Xp22.31. Deletions encompassing this region are associated with Xp22.3 microdeletion syndrome. This aberration may be involved in disease pathogenesis in your patient.**

chromosomal region	type of imbalance	size	ISCN (2020)	microdeletion syndrome	chromosomal region
Xp22.31	**deletion (0 copies)**	**1.6 Mb**	**arr[hg19] Xp22.31(6489877_8131810)x0**	**Xp22.3 microdeletion syndrome**	**Xp22.31**

INTERPRETATION

Xp22.31 (1.6 Mb):

In your patient we detected the approx. 1.6 Mb deletion on the short arm of chromosome X in a hemizygous state. Deletions encompassing this region are causative for the Xp22.3 microdeletion syndrome. The corresponding phenotype is highly variable (depending on length of deletion) and is mainly characterized by ichthyosis, mild-moderate intellectual deficit, Kallmann syndrome, short stature, chondrodysplasia punctata, and ocular albinism. Epilepsy, attention deficit-hyperactivity disorder, autism, and difficulties with social communication can be associated (ORPHA:1643; Gohlke et al., 2000, PMID: 10922387). This microdeletion contains the gene *STS* which is associated with steroid sulphatase deficiency (STS; DECIPHER CNV Syndrome; OMIM #308100). In the DECIPHER database similar losses were, beside other symptoms, observed in patients with delayed speech and language development, seizures, and an

abnormal facial shape (e. g. patients 338884, 276056, 339534). They were present in a hemizygous or heterozygous state and were inherited or occurred *de novo*.

Based on the available data this variant is classified as pathogenic and causative for Xp22.3-deletion syndrome. It may be involved in disease pathogenesis in your patient.

GENETIC RELEVANCE

Your patient is hemizygous for a pathogenic deletion. This variant will be inherited to every female offspring. Male offspring do not inherit this allele.

RECOMMENDATION

In order to determine whether the detected deletion is *de novo* in your patient or inherited, we recommend segregation analysis of the patient's mother regarding this variant.

As the cause of disease remains unclear, we will now continue with the requested panel diagnostics.

According to § 10 of the German Genetic Diagnostics Legislation, appropriate genetic counseling should be offered with all diagnostic genetic testing. Following the identification of the molecular cause of a genetic disease, genetic counseling has to be offered.

Medical report written by: Scientist 1

Proofread by: Scientist 2

With kind regards,

Dr. med. Dr. rer. nat. Saskia Biskup
Dr. med. Friedmar Kreuz, M.A.

Consultant for Human Genetics

Dr. rer. nat. Heinz-Dieter Gabriel
PD Dr. biol. hum. Christiane Maier
Dr. rer. nat. Christian Wilhelm
Dr. rer. nat. Martin Ritthaler

Diagnostics

ADDITIONAL INFORMATION

Methods Array comparative genomic hybridisation was performed using the Agilent Sureprint G3 Unrestricted CGH ISCA 180k microarray. It contains 180,000 probes providing complete coverage of the human genome and a practical resolution of 100 kb. The data was aligned to the reference genome described in NCBI Human Genome Build 19 and analyzed with CytoGenomics software v5.0 (Agilent). Databases used for the evaluation of detected variants include DECIPHER, DGV, ClinVar and gnomAD SV. Deletions and duplications classified as benign or likely benign based on current knowledge will not be reported. Genes were screened for clinical and functional relevance and listed in detail only if they might be clinically related to the patient's phenotype at the time of analysis. Carrier status for recessive diseases not directly related to the clinical phenotype is not reported. Variants are named according to ISCN guidelines (2020). Array-CGH will not detect balanced rearrangements, point mutations or low-level mosaicism. Aberrations on the Y chromosome and in the pseudoautosomal region (PAR) cannot be detected with high accuracy. The integration site of duplications cannot be determined by array-CGH analysis.

A list of all analysed copy number variants is available upon request.

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).

Communication, dissemination and usage of this report for scientific purposes is only permitted in accordance with the German Genetic Diagnostics Legislation.

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