



Institut für Humangenetik
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cc: [consultant board certified medical doctor in human genetics]

Leipzig, xx.xx.xxxx, ToK

Results within the research project "Mosaicism and risk prediction for parents of children with *de novo* variants"

[surname, first name], *00.00. 0000 [♀/♂] (Index)	LaborNr: 00000000-00000000-00000000
	Sample entry: 00.00.0000 Date of request: 00.00.0000

Results: No evidence of a mosaic regarding the previously known variant NM_007327.4:c.1972G>T, (p.Asp658Tyr) in the *GRIN1* gene was found in various tissue samples from both parents

Dear [Surname] family,

Our study found no evidence of a mosaic in the analysed tissue samples from either parent related to the disease diagnosed in your child. However, we would like to point out that these are research findings that have not yet been validated by an independent research group. If needed, genetic counselling is available (in person or by phone). You can request an appointment at mosaike@medizin.uni-leipzig.de.

If you have any questions, please feel free to contact us by phone [phonenumber] or email [email].

Best regards

[surname, first name]
board certified medical doctor in human genetics

[surname, first name]
board certified medical doctor in human genetics

Methods

Amplicon-spike in using NGS

The position of the variant known to exist in the family is amplified using primers to produce an amplicon of approximately 350–600 bp. The product is then loaded onto a lane of an S4 flowcell at a concentration of 0.1% per sample and sequenced on an Illumina NovaSeq 6000. The DNA is sequenced at ultra-high depth, meaning that the position of the variant is covered very extensively (>40,000 reads). A bioinformatics pipeline is then applied to determine whether the variant is present in the sample and, if so, at what frequency. The result is evaluated both as a naive count of the alternative allele frequency and following the application of a statistical model (Bayesian method). Within the Bayesian method, the most probable allele frequency is estimated, taking into account an error rate. The determined allele fraction may therefore differ slightly from the actual allele fraction.

This method is not a standard procedure and is used by us exclusively for research purposes. It has not been validated by the results of independent research carried out by other research groups.

Die Informationen auf dieser Seite sind essentiell und für Laien möglichst verständlich dargestellt. Nach §10 und §15 Gendiagnostikgesetz (GenDG) muss zur Mitteilung des Befundes der genetischen Untersuchung eine genetische Beratung angeboten werden.

Aufsichtsratsvorsitzender: Prof. Dr. Dr.h.c.mult. Wolfgang Holzgreve, MBA
Medizinischer Vorstand und Sprecher des Vorstandes: Prof. Dr. Christoph Josten
Kaufmännischer Vorstand: Dr. Robert Jacob

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Results within the research project "Mosaicism and risk prediction for parents of children with de novo variants"

[surname, first name], *00.00.0000 [♀/♂] (Index)	LaborNr: 0000000-0000000-0000000
[surname, first name], *00.00.0000 (father)	LaborNr: 0000000-0000000-0000000
	Sample entry: 00.00.0000
	Date of request: 00.00.0000

results:	Evidence of a mixed mosaicism with regard to the previously known variant c.3560G>C, p.(Arg1187Pro) in the CHD3 gene in various tissue samples from the father
further aspects:	The risk of recurrence of Snijders Blok-Campeau syndrome, associated with CHD3, is increased in the offspring of Mr [firstname surname]. We recommend genetic counselling, particularly if you are planning to have children.

Dear [Surname] family,
In our study, a mixed mosaicism was detected in the blood, buccal swab, hair and semen samples taken from the father in relation to the condition diagnosed in your child. There is therefore an increased risk (>1%) of recurrence in Mr [Surname]'s offspring with regard to CHD3-associated Snijders-Blok-Campeau syndrome.

gene, OMIM, inheritance	variant(s)	tissue samples examined	allele fraction
CHD3 Snijders Blok-Campeau syndrome (#618205) autosomal dominant	17:7903336 NM_001005273.3 c.3560G>C p.(Arg1187Pro)	blood of the mother	0 %
		buccal swab of the mother	0 %
		hair of the mother	0 %
		blood of the father	2,1 %
		buccal swab of the father	1,8 %
		hair of the father	0,5 %
		semen sample of the father	11,0 %

This pathogenic variant had previously been detected as heterozygous in the child (our medical report dated 00.00.0000).
Please note that these are research results that have not yet been validated by an independent research group. We recommend genetic counselling (in person or by telephone). You can request an appointment at [email]. If you have any further questions, please do not hesitate to contact us by telephone [phonenumber] or by email [email].
With kind regards

[surname, first name]
board certified medical doctor in human genetics

[surname, first name]
board certified medical doctor in human genetics

Methods
Amplicon-based spike-in using NGS

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Combined cohorts with Neuser *et al.* 2025 (total cohort, mosaic cases, phasing)

	Neuser et al. (2025)	our data	total
total cohort	135	64	198
mosaic cases	6/135 (4.4%)	7/64 (10.9%)	13/198 (6.6%)
paternal isolated semen mosaic	2/6 (33.3%)	4/7 (57.1%)	6/13 (46.2%)
of total cohort	2/135 (1.5%)	4/64 (6.3%)	6/198 (3.0%)
paternal mixed mosaic	2/6 (33.3%)	1/7 (14.3%)	3/13 (23.1%)
of total cohort	2/135 (1.5%)	1/64 (1.6%)	3/198 (1.5%)
maternal mixed mosaic	2/6 (33.3%)	2/7 (28.6%)	4/13 (30.8%)
of total cohort	2/135 (1.5%)	2/64 (3.1%)	4/198 (2.0%)
phasing paternal (of successfully phased variants)	63/81 (77.8%)	39/42 (92.9%)	102/123 (82.9%)
phasing maternal (of successfully phased variants)	18/81 (22.2%)	3/42 (7.1%)	21/123 (17.1%)