UNIKLINIK KÖLN | Institut für Humangenetik

Certified by: TÜV SÜD ISO 9001

PATIENT (use sticker if available)

Last name: _____

First name(s): _____

Date of birth: _____ gender: m ☐ f ☐

Address: _____

_____

Ethnic background: _____
(may be important for recessive conditions)

☐ **urgent**

Pregnancy? ☐ yes ☐ no

Pregnent person: _____

Week of gestation: _____

Please ship samples to:

Institute of Human Genetics
University Hospital of Cologne
Kerpener Str. 34
50931 Cologne, Germany

Phone +49-221-478-86811
Fax +49-221-478-86812

Billing

Test will be paid by ☐ Referring facility ☐ Patient

Please note that international requests must be accompanied by a confirmation of payment. Please contact us for details.

Informed consent form

(according to German Genetic Diagnostics Act)

The planned genetic test, its limitations and possible interpretations of results have been explained to me in detail by the physician stated below. I have had the opportunity to discuss the details and ask questions about this information. By signing this form, I consent that genetic testing will be performed for the following disease/condition/diagnosis (to be entered by physician):

_____

I consent that the required sample (e.g. blood, tissue, amniotic fluid) will be taken.
The sample and the results of the testing may be used as follows:

I consent that **remaining sample material** will be **stored** for verification of results and quality management purposes.
I consent that **remaining sample material** will be **stored** to be available for new diagnostic options in the future.
I consent that the **test results and records** will not be destroyed after 10 years — as laid down in German statutory provisions — but will be **stored**.
I consent that the request for testing and all personal details required for the testing are **forwarded** to a specialized cooperating laboratory if necessary .
I wish to be informed on **incidental findings** that may be discovered by the genetic testing, even if they do not directly relate to the above mentioned disease/condition/diagnosis in question.
I consent that **remaining sample material** will be used for **research on the causes** and improved treatment of genetic diseases.
I consent that **data/results** that may be generated on the condition in question will be used in de-identified (pseudonymized) form for **academic or medical teaching** and for **scientific purposes** and will be published in anonymized form in **scientific journals**.
I consent that the results of the testing may be sent to the following physicians: _____

- Please delete as appropriate -

I am free to withdraw any of the above statements at any time. I have had enough time to consider my decision.

☐ I obtained an informend consent form signed by the patient.

Place, Date	Signature Patient/ Parent/Legal Guardian	Name of Physician in printed characters	Stamp and Signature of Physician
_____	_____	_____	_____

►Please give a copy of the completed and signed consent form to the patient◄

Request for molecular genetic testing —
Noonan syndrome and hypertrophic cardiomyopathy

Clinical Findings / Diagnosis / Indication / Reason for Testing

Has any previous genetic test been performed in the patient relating to the above reason for testing?

☐ no

☐ yes, please specify previous findings / genetic tests:

Is there an Index patient known?

☐ no

☐ yes (please specify mutation, disorder and relationship)

☐ yes; but there are no or incomplete information on the index patient. In this case a specific reason has to be given for the genetic mutation analysis on your patient. The statement **must** include the probability of predisposition of your patient or the remaining lifetime risk of developing the disease.

Type of testing

☐ diagnostic testing

☐ diagnostic testing - segregation analysis in the parents/further family members if the test result of the child/index patient requires clarification

☐ prenatal testing

☐ predictive testing

☐ heterozygosity/carrier testing

Type of sample

☐ blood

☐ DNA

☐ buccal swab

☐ saliva

☐ fibroblasts

☐ chorion villi

☐ amniotic fluid

☐ other:

Date of sample collection

sample was collected on:

Family history / Pedigree

☐ significant family history (see above information on index patient)

☐ mother clearly affected

☐ father clearly affected

☐ family history not available

☐ no significant family history

☐ both parents clearly not affected

☐ mother clearly not affected,
no information on father available

☐ father clearly not affected,
no information on mother available

Parental consanguinity

☐ no

☐ yes (please specify):

Pedigree (optional)

Request for molecular genetic testing — Noonan syndrome and hypertrophic cardiomyopathy

You can choose between standard panels, complete panels or single gene diagnostics. Standard panels combine the genes most frequently mutated in patients with the respective phenotype and contain up to 25 kb of coding sequence (only relevant for patients with the E112 [S2] health insurance document). Complete panels cover all genes associated with the phenotype. If mutations of a single gene are known to be causative for a large proportion of the phenotype, the gene may be analyzed by conventional Sanger sequencing prior to an NGS-analysis.

Contact person for clinical questions: Prof. Dr. med. C. Netzer (+49 221-478-89586, christian.netzer@uk-koeln.de). For all other questions related to genetic diagnostics, sample material and billing, please contact: +49 221-478-86811 and +49 221-478-86193 or mvz-humangenetik@uk-koeln.de.

Multi-gene panel diagnostics:
„**Core-Gene**" of panels are printed in **bold**; the coding sequence of these genes has to be analysed to 100% in the highest quality.
*: for these genes a quantitative analysis by MLPA is also available.

Hypertrophic cardiomyopathy (HCM)

☐ **Standard panel (#001): Main genes for HCM according to ESC Guidelines 2014, except TTN**

ACTC1, CSRP3, GLA, LAMP2, MYBPC3, MYH7, MYL2, MYL3, PLN, PRKAG2, TNNI3, TNNT2, TPM1 (13 genes, 19.2 kb)

☐ **Complete panel (#002): Main genes for HCM according to ESC Guidelines 2014, complete**

ACTA1, ***ACTC1****, CRYAB,* ***CSRP3****, DES, FHL1,* ***GLA****,* ***LAMP2****,* ***MYBPC3, MYH7, MYL2, MYL3, PLN, PRKAG2****,* ***TNNI3, TNNT2, TPM1, TTN,*** *TTR* (19 genes, 123.8 kb)

☐ **Complete panel (#138): All HCM-associated genes according to ESC Guidelines 2014**

A2ML1, AARS2, ACAD9, ACADVL, ACTA1, ***ACTC1****, ACTN2, AGK, AGL, AGPAT2, ATPAF2, BRAF, BSCL2, COQ2, COX6B1, CRYAB,* ***CSRP3****, DES, DLD, FAH, FLNC, FHL1, FXN, GAA, GFM1,* ***GLA****, GLB1, GNPTAB, GUSB, HRAS, KRAS,* ***LAMP2****, LIAS, LZTR1, MAP2K1, MAP2K2, MLYCD, MRPL3, MRPS22, MTO1,* ***MYBPC3****,* ***MYH7****,* ***MYL2****,* ***MYL3****, MYOZ2, NF1, NRAS, PDHA1, PHKA1,* ***PLN****, PMM2,* ***PRKAG2****, PTPN11, RAF1, RASA2, RIT, RRAS, SLC22A5, SOS1, SOS2, SURF1, TMEM70, TNNC1,* ***TNNI3****,* ***TNNT2****,* ***TPM1****, TSFM,* ***TTN****, TTR* (69 genes, 223.5 Kb)

☐ **Standard panel (#004): HCM due to mitochondrial deficiencies according to ESC Guidelines 2014**

ACAD9, AGK, ATPAF2, COQ2, COX6B1, FXN, LIAS, PDHA1, SURF1, TMEM70 (10 genes, 10.2 kb)

☐ **Standard Panel (#005): Fatal infantile HCM due to mitochondrial deficiencies according to ESC Guidelines 2014**

AARS2, GFM1, MRPL3, MRPS22, MTO1, TSFM (6 genes, 10.5 kb)

☐ **Complete panel (#006): HCM due to metabolic disorders according to ESC Guidelines 2014**

ACADVL, AGL, AGPAT2, BSCL2, DLD, FAH, GAA, GLB1, GNPTAB, GUSB, MLYCD, PHKA1, PMM2, SLC22A5 (14 genes, 29.6 kb)

☐ **Complete panel (#007): RASopathies with HCM according to ESC Guidelines 2014**

A2ML1, BRAF, HRAS, KRAS, LZTR1, MAP2K1, MAP2K2, NF1, NRAS, ***PTPN11,*** *RAF1, RASA2, RIT, RRAS, SOS1, SOS2*
(16 genes, 37.3 kb)

☐ **Single gene diagnostics**

☐ *ACTA1* ☐ *MYH7* ☐ *TNNT2*
☐ *MYBPC3* ☐ *TNNI3* ☐ *TPM1*

Noonan syndrome

☐ ***PTPN11*-single gene diagnotic (#057): First diagnostic step according to German EBM 11355**

PTPN11 (1 gene, 1.8 kb)

☐ **Standard panel (#008): All other genes associated with Noonan syndrome, second diagnostic step, genes according to Genereviews**

A2ML1, ***BRAF, KRAS****, LZTR1, MAP2K1, NRAS,* ***RAF1****, RASA2,* ***RIT****, RRAS,* ***SOS1****, SOS2* (12 genes, 25.65 kb)

☐ **Standard panel (#009): All genes associated with Noonan syndrome according to Genereviews, without stepwise diagnostics (in urgent cases)**

A2ML1, ***BRAF, KRAS****, LZTR1, MAP2K1, NRAS,* ***PTPN11****,* ***RAF1****, RASA2,* ***RIT****, RRAS,* ***SOS1****, SOS2* (13 gened, 27.1 kb)

☐ **Single gene diagnostics**

☐ *PTPN11*
☐ *RIT*

Request for molecular genetic testing — Noonan syndrome and hypertrophic cardiomyopathy

You can choose between the complete panel *Noonan Snydrom and hypertrophic cardiomyopathy* or single gene diagnostics.

Contact person for clinical questions: Prof. Dr. med. C. Netzer (+49 221-478-89586, christian.netzer@uk-koeln.de). For all other questions related to genetic diagnostics, sample material and billing, please contact: +49 221-478-86811 and +49 221-478-86193 or mvz-humangenetik@uk-koeln.de.

Multi-gene panel diagnostics:
*: for these genes a quantitative analysis by MLPA is also available.

☐ **Complete panel *Noonan syndrome and hypertrophic cardiomyopathy* (#138)**

☐ **Single gene diagnostics by Sanger-sequencing technology**

Gene	kb	Single gene diagnostics
A2ML1	4.365	not available
AARS2	2.958	not available
ACAD9	1.866	not available
ACADVL	1.968	not available
ACTA1	1.134	☐
ACTC1	1.134	not available
ACTN2	2.685	not available
AGK	1.269	not available
AGL	4.599	not available
AGPAT2	0.837	not available
ATPAF2	0.87	not available
BRAF	2.301	not available
BSCL2	1.197	not available
COQ2	1.266	☐
COX6B1	0.261	not available
CRYAB	0.528	not available
CSRP3	0.585	not available
DES	1.413	not available
DLD	1.53	not available
FAH	1.26	not available
FLNC	8.178	not available
FHL1	0.843	not available
FXN	0.633	not available
GAA	2.859	not available
GFM1	2.256	not available
GLA	1.29	not available
GLB1	2.034	not available
GNPTAB	3.771	not available
GUSB	1.956	not available
HRAS	0.57	not available
KRAS	0.567	not available
LAMP2	1.236	not available
LIAS	1.119	not available
LZTR1	2.523	not available
MAP2K1	1.182	not available
MAP2K2	1.203	not available
MLYCD	1.482	not available
MRPL3	1.047	not available
MRPS22	1.083	not available

Gene	kb	Single gene diagnostics
MTO1	2.154	not available
MYBPC3	3.825	☐
MYH7	5.808	☐
MYL2	0.501	not available
MYL3	0.588	not available
MYOZ2	0.795	not available
NF1	8.457	not available
NRAS	0.57	not available
PDHA1	1.194	not available
PHKA1	3.672	not available
PLN	0.159	not available
PMM2	0.741	not available
PRKAG2	1.71	not available
PTPN11	1.782	☐
RAF1	1.947	not available
RASA2	2.55	not available
RIT1	0.66	☐
RRAS	0.657	not available
SLC22A5	1.674	not available
SOS1	4.002	not available
SOS2	3.999	not available
SURF1	0.903	not available
TMEM70	0.783	not available
TNNC1	0.486	not available
TNNI3	0.633	☐
TNNT2	0.867	☐
TPM1	0.855	☐
TSFM	1.041	not available
TTN	100.272	not available
TTR	0.444	not available