

Questionnaire for the participation in the study
“Description of the clinical phenotype of adults with rare genetic syndromes”

Name the participant (in capital letters): _____

Date of birth: _____

This page is intended for pseudonymization. Solely the person in charge of pseudonymization will have access to the information on this first page.

Pseudonym (will be completed by the study team): _____

Has the participant been published previously?

☐ Yes

☐ No

If yes, which publication and pseudonym?

Coordinates of the doctor completing the questionnaire:

Name of the doctor: _____

Affiliation of the doctor: _____

Email address of the doctor: _____

If we are also allowed to contact another person again for further information, please indicate:

Name of the contact person: _____

Email address of the contact person: _____

AFTER PSEUDONYMIZATION, THIS PAGE IS KEPT SEPARATE FROM THE REST OF THE QUESTIONNAIRE

1. **Genetic findings**

Indication for genetic testing: _____

Age of the participant at clinical diagnosis of the syndrome: _____

Age of the participant at molecular diagnosis of the syndrome: _____

(Age at which the genetic analysis confirmed the diagnosis of the participant)

In which gene has the causal mutation been identified? _____

If you have difficulties, completing the genetic information below, you can add the genetic report(s) of the participant instead.

Transcript of the mutated gene (NM_ or ENST_ Number): _____

Variant at DNA level (c.): _____

Variant at Protein level (p.): _____

Genomic position of the variant: _____

Used reference genome (e.g. hg19): _____

Variant detected as: ☐ homozygous ☐ heterozygous ☐ mosaic (percentage: _____)

Origin of the variant:

- ☐ *de novo* (not inherited maternally or paternally)
- ☐ inherited maternally
- ☐ inherited paternally
- ☐ both parents not tested
- ☐ not maternally, father not tested
- ☐ not paternally, mother not tested

Methods used for diagnosis:

- ☐ direct gene sequencing
- ☐ multi gene panel analysis
- ☐ exome sequencing
- ☐ other, please mention: _____

Has a chromosomal analysis been performed?

- ☐ Yes
- ☐ No

If yes, please indicate the results: _____

Has a microarray analysis been performed?

- ☐ Yes
- ☐ No

If yes, please indicate the results: _____

Are there any other relevant genetic findings?

- ☐ Yes
- ☐ No

If yes, please describe: _____

2. **General Data**

Current age of the participant: _____ years, _____ months

Gender of the participant:

☐ female

☐ male

Country: _____

Age at last measurement: _____ years _____ month

Height in cm (and SD): _____ Calculated target height in cm: _____

If the participant has failure to thrive, please indicate age at onset: _____

Weight in kg (and SD): _____

BMI in kg/m²: _____

If the participant is overweight (BMI > 25 kg/m²) or underweight (BMI < 18,5 kg/m²),
please indicate age at onset: _____

OFC in cm (and SD): _____

If the participant has micro- ($\leq -2SD$) or macrocephaly ($\geq +2SD$), please indicate age
at onset: _____

Are other family members affected with the same syndrome?

☐ Yes

☐ No

If yes, please indicate their relationships: _____

3. **Clinical Data**

Prenatal and perinatal history

Were there any abnormalities during pregnancy?

☐ Yes → Please describe: _____

☐ No

☐ Information not available anymore

Were there any problems during birth?

☐ Yes → Please describe: _____

☐ No

☐ Information not available anymore

Was the participant born at term?

☐ Yes

☐ No

☐ Information not available anymore

Please indicate the gestational age (weeks and days) at birth: _____

Birth length in cm (and SD): _____

Birth weight in g (and SD): _____

Birth OFC in cm (and SD): _____

Development

Does the participant have intellectual disability?

- ☐ Yes → please select: ☐ mild ☐ moderate ☐ severe
☐ No

Did the participant get an IQ-test?

- ☐ Yes → please indicate the full scale IQ: _____
☐ No → please try to estimate the full scale IQ (see table below): _____

MR Level	Description (IQ)	Adult phenotype
0	Normal	No mental retardation (MR)
1	Borderline (<70)	Attends standard school for many years; requires minor/major support
2	Very mild (<65)	Attends standard school for a few years; requires major support; has simple reading, writing, and math ability
3	Mild (<50)	Understands everything, including long sentences; has very simple reading, writing, and math ability
4	Moderate (<35)	Understands almost everything; makes use of small sentences and lots of signs
5	Severe (<20)	Understands simple, daily sentences and single words; uses sentences of 2–3 words, and many signs; walks
6	Very severe (<10)	Understands a few words; usually walks, unsteadily, if supported; has no language or only a few words
7	Profound	Shows minor or no response; may sit and stand unaided; walking is rare

Following Zhang et al 2005

At what age was the participant able to sit without help (age in months): _____

At what age was the participant able to walk without help (age in months): _____

At what age did the participant speak first words (age in months): _____

At what age was a developmental delay diagnosed (age in months): _____

What are the current communication abilities?

- ☐ the participant is unable to communicate his wants and needs
☐ the participant uses sounds but no spoken words
☐ the participant uses gestures
☐ the participant uses sign language
☐ the participant uses alternative communication aids, please indicate: _____
☐ the participant speaks fluently

If none of these options fit, please describe: _____

What are the current speech abilities?

- ☐ sounds but no spoken words
☐ only simple words
☐ two-word sentences (e.g. come here, be hungry,...)
☐ simple full sentences (e.g. I am hungry,...)
☐ the participant is able to tell a story

What are the current reading abilities?

- ☐ none
- ☐ recognizes some simple words
- ☐ simple storybook
- ☐ reads books for children aged: _____
- ☐ reads newspapers and books

What are the current writing abilities?

- ☐ none
- ☐ writes single letters
- ☐ writes her/his name
- ☐ writes some simple words
- ☐ copies a sentence
- ☐ writes a sentence independently
- ☐ writes a letter

Does the participant need help with the daily hygiene (showering, putting on clothes, brushing teeth,...)?

- ☐ Yes
- ☐ No

Does the participant need help with eating?

- ☐ Yes
- ☐ No

What are the participants' cooking abilities?

- ☐ none
- ☐ simple tasks, e.g. makes toast
- ☐ is able to heat up food in the microwave/oven
- ☐ is able to cook a meal (e.g. pasta)

What school degree did the participant achieve?

- ☐ regular education, please indicate a degree if possible: _____
- ☐ special education, please indicate a degree if possible: _____

Does the participant have an occupation?

- ☐ Yes → please indicate the occupation: _____
- ☐ No

Is the participant able to live independently?

- ☐ Yes
- ☐ No

Regression

Has the participant experienced any regression in her/his abilities?

- ☐ Yes → please indicate the age at regression: _____
- ☐ No

If yes, please select and describe:

- ☐ the participant lost verbal abilities: _____

- ☐ the participant lost motor abilities: _____
- ☐ other: _____

Behavioral anomalies

Does the participant have behavioral anomalies? Please select.

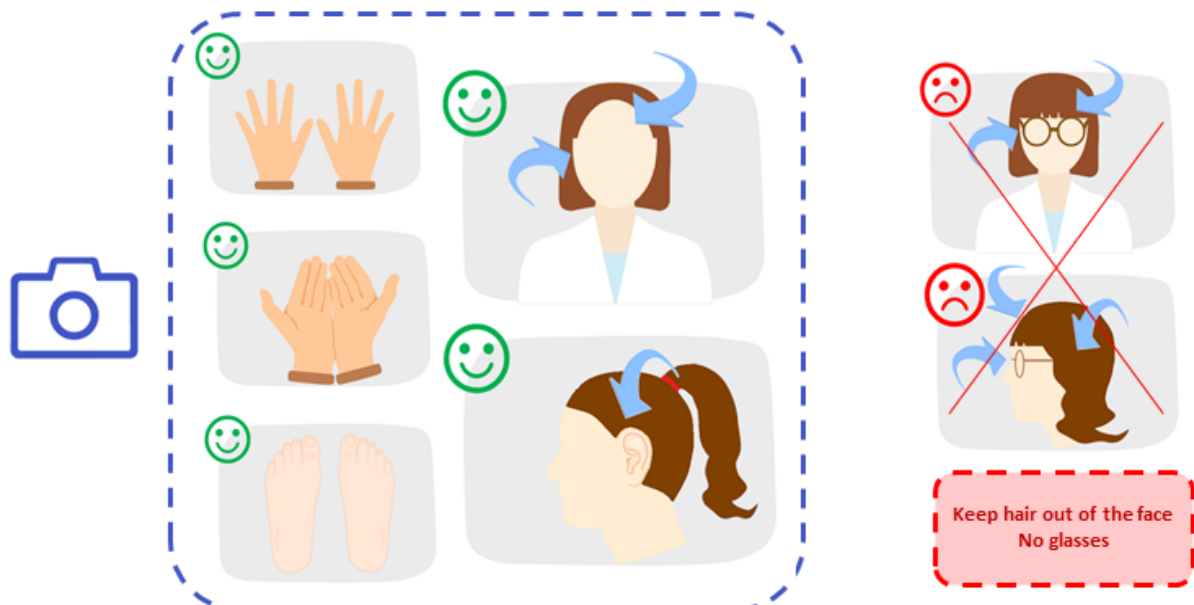
- ☐ Autism
- ☐ Aggressive behavior
- ☐ Attention deficit/hyperactivity disorder
- ☐ Stereotypic movements
- ☐ Sleeping difficulties
- ☐ Sensitivity to many or specific stimuli, please describe: _____
- ☐ Other, please describe: _____

4. Dysmorphic features

Does the participant have marked facial similarities to other participants with the syndrome?

- ☐ Yes
- ☐ No

Alternatively, if the participant/legal guardian agreed to the use of photographs, you can add photographs of the participant: photographs from the face in front view and side view (without glasses), hands and feet. This would help us to make uniformed descriptions of de dysmorphologic features of the participants. Childhood photographs of the participant are also welcome and might allow for evaluation of progressive dysmorphic features.



In the following tables, please check the boxes with matching terms

Head

Cranium:	<input type="checkbox"/> brachycephaly <input type="checkbox"/> other: _____	<input type="checkbox"/> dolichocephaly	<input type="checkbox"/> turriccephaly
Face:	<input type="checkbox"/> broad <input type="checkbox"/> trigulated	<input type="checkbox"/> flat <input type="checkbox"/> hypotonic	<input type="checkbox"/> coarse <input type="checkbox"/> other: _____
Hairline:	<input type="checkbox"/> low posterior <input type="checkbox"/> other: _____	<input type="checkbox"/> low anterior	<input type="checkbox"/> high anterior <input type="checkbox"/> frontal balding
Forehead:	<input type="checkbox"/> sloping <input type="checkbox"/> bossing	<input type="checkbox"/> narrow <input type="checkbox"/> other: _____	<input type="checkbox"/> broad <input type="checkbox"/> prominent
Cheeks:	<input type="checkbox"/> underdeveloped bones <input type="checkbox"/> other: _____	<input type="checkbox"/> prominent bones	<input type="checkbox"/> full <input type="checkbox"/> sunken
Midface:	<input type="checkbox"/> retrusion	<input type="checkbox"/> prominence	<input type="checkbox"/> other: _____
Chin:	<input type="checkbox"/> microgathia <input type="checkbox"/> retrogathia	<input type="checkbox"/> narrow <input type="checkbox"/> others: _____	<input type="checkbox"/> broad <input type="checkbox"/> prognathism
Neck:	<input type="checkbox"/> broad <input type="checkbox"/> other: _____	<input type="checkbox"/> long	<input type="checkbox"/> short <input type="checkbox"/> webbing
Upper lip:	<input type="checkbox"/> absent Cupid's bow <input type="checkbox"/> tented	<input type="checkbox"/> exaggerated Cupid's bow <input type="checkbox"/> everted	<input type="checkbox"/> thick <input type="checkbox"/> thin <input type="checkbox"/> other: _____
Lower lip:	<input type="checkbox"/> everted	<input type="checkbox"/> thin	<input type="checkbox"/> thick <input type="checkbox"/> other: _____
Mouth:	<input type="checkbox"/> narrow	<input type="checkbox"/> wide	<input type="checkbox"/> other: _____
Oral cavity:	<input type="checkbox"/> protuding tongue	<input type="checkbox"/> narrow palate	<input type="checkbox"/> high palate <input type="checkbox"/> other: _____
Nose:	<input type="checkbox"/> depressed nasal bridge <input type="checkbox"/> broad nasal tip	<input type="checkbox"/> anteverted nares <input type="checkbox"/> other: _____	<input type="checkbox"/> bulbous nose <input type="checkbox"/> narrow nasal tip
Philtrum:	<input type="checkbox"/> broad <input type="checkbox"/> smooth	<input type="checkbox"/> narrow <input type="checkbox"/> deep	<input type="checkbox"/> long <input type="checkbox"/> short <input type="checkbox"/> other: _____
Eyes:	<input type="checkbox"/> blepharophimosis <input type="checkbox"/> hypertelorism <input type="checkbox"/> strabism	<input type="checkbox"/> epicanthus <input type="checkbox"/> proptosis <input type="checkbox"/> other: _____	<input type="checkbox"/> deep set <input type="checkbox"/> ptosis <input type="checkbox"/> hypotelorism <input type="checkbox"/> telecanthus
Palpebral fissures:	<input type="checkbox"/> almond shaped <input type="checkbox"/> upslanted	<input type="checkbox"/> long <input type="checkbox"/> other: _____	<input type="checkbox"/> short <input type="checkbox"/> downslanted
Eyebrows:	<input type="checkbox"/> highly arched <input type="checkbox"/> other: _____	<input type="checkbox"/> horizontal	<input type="checkbox"/> thick <input type="checkbox"/> synophrys

Please, note the features which became more prominent over time: _____

Childhood photographs of the participant are also welcome and might allow for evaluation of progressive dysmorphic features.

Extremities

Hands:	<input type="checkbox"/> clinodactyly of the 5th finger <input type="checkbox"/> arachnodactyly <input type="checkbox"/> hypoplastic thumbs <input type="checkbox"/> single transverse palmar crease <input type="checkbox"/> other: _____	<input type="checkbox"/> tapered fingers <input type="checkbox"/> brachydactyly <input type="checkbox"/> prominent digit pad <input type="checkbox"/> hyperextensible fingers	<input type="checkbox"/> deep palmar creases <input type="checkbox"/> camptodactyly <input type="checkbox"/> postaxial polydactyly <input type="checkbox"/> prominent interphalangeal joints	<input type="checkbox"/> decreased palmar creases <input type="checkbox"/> clubbing <input type="checkbox"/> preaxial polydactyly
Feet:	<input type="checkbox"/> preaxial polydactyly <input type="checkbox"/> pes planus	<input type="checkbox"/> postaxial polydactyly <input type="checkbox"/> sandal gap	<input type="checkbox"/> rocker bottom foot <input type="checkbox"/> other: _____	<input type="checkbox"/> pes cavus

Other findings

Thorax:	<input type="checkbox"/> small <input type="checkbox"/> pectus excavatum <input type="checkbox"/> Pectus carinatum <input type="checkbox"/> accessory nipples
Abdomen:	<input type="checkbox"/> umbilical hernia <input type="checkbox"/> Inguinal hernia
Back:	<input type="checkbox"/> scoliosis
Other:	

5. Medical issues

In your eyes, what is the greatest health issue of the participant? _____

Has the participant ever had surgery?

- ☐ Yes
☐ No

If yes, please indicate the type of surgery and the age of the participant at surgery for all interventions: _____

Neurologic issues

Has a brain CT/MRI been performed?

- ☐ Yes → please indicate or add the results: _____
☐ No

Has the participant had EEGs (electroencephalography)?

- ☐ Yes → please indicate the results: _____
☐ No

Has the participant been diagnosed with epilepsy?

- ☐ Yes → what was the age at first seizures: _____
- ☐ No

If yes, the participant has epilepsy please indicate:

- Type of seizures: _____
- Antiepileptic medication: _____
- The last time she/he had seizures: _____
- The average number of seizures per time period: _____/month
_____/week
- The average duration of a seizure: _____
- How many times has the participant had status epilepticus? _____

Does the participant have muscular hypotonia?

- ☐ Yes
- ☐ No

Please indicate, if the participant has any other neurological problems with age of onset:

Cardiovascular issues

Has the participant had any anomalies of the heart or vessels since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any issues of the heart or vessels over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Respiratory issues

Has the participant had any anomalies of the lungs and airways since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any issues of the lungs and airways over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Gastro-intestinal issues

Has the participant experienced feeding problems in his childhood?

- ☐ Yes → From which age until which age?: _____
- ☐ No

If yes, was G-Tube feeding necessary and for how long? _____

Has the participant had any anomalies of the digestive system since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any issues of the digestive system over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Nephrological issues

Has the participant had any anomalies of the kidney since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any kidney issues over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Urogenital issues

Has the participant had any anomaly of the bladder, urine tract or genitals since birth e.g. hypospadias, cryptorchism?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any bladder, urinary tract or genital issues over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Endocrine issues

Has the participant had any endocrine anomalies since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any endocrine issues over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Was the puberty in any way remarkable (precocious/delayed/others)?

- ☐ Yes → please describe: _____
- ☐ No

If applicable age by menarche (in years): _____

Dermatological issues

Has the participant had any anomalies of the skin since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any skin issues over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Ectodermal issues

Please select the features present in the participant:

- ☐ Hypertrichosis (many hairs in abnormal sites), please indicate age of onset: _____
- ☐ Sparse hair, please indicate age of onset: _____
- ☐ Nail hypoplasia/aplasia, please indicate which fingers, toes: _____
- ☐ Delayed tooth eruption, please indicate age: _____
- ☐ Delayed loss of primary teeth, please indicate age: _____
- ☐ Missing teeth (oligodontia), please indicate which teeth: _____
- ☐ Other hair, nail or teeth anomalies, please describe: _____

Eye issues

Has the participant had any anomaly of the eye/vision since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any eye/vision issues over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Please indicate current vision ability: _____

Ear/Hearing issues

Has the participant had any anomaly of the ear/hearing since birth?

- ☐ Yes → please indicate: _____
- ☐ No

Has the participant developed any ear/auditive issues over the years?

- ☐ Yes → please indicate type and age of onset: _____
- ☐ No

Hematological and neoplastic diseases

Has the participant any hematological anomalies?

- ☐ Yes → please indicate the anomaly and age of onset: _____
- ☐ No

Has the participant had any tumors or cancer (neoplasm)?

- ☐ Yes → please indicate the type and age at diagnosis: _____
- ☐ No

Is the participant more susceptible to infections?

- ☐ Yes
- ☐ No

Musculoskeletal issues

Does the participant have any anomaly of the muscles, bones and joints since birth?

- ☐ Yes → please indicate: _____
☐ No

Has the participant developed any issues of the muscles, bones or joints over the years?

- ☐ Yes → please indicate type and age of onset: _____
☐ No

6. Therapies

Please indicate which therapies (also drugs) the participant is receiving or has received and since what age:

7. Comments

If there are other important clinical findings, please comment:

We thank you for taking the time to filling in the questionnaire!
Please, join the consent form for this study and if necessary medical reports.

In addition, if the participant/legal guardian gave consent, photographs from the face in front view and side view (without glasses), hands and feet of the participant would be very much appreciated and would allow us a uniformed description of the participants.