



Indications

Connective tissue disorders

Please note: Send only EDTA blood unless otherwise indicated.

- Marfan syndrome; Loeys-Dietz syndrome; TAAD
 - FBN1
 - TGFBR1
 - TGFBR2
 - SMAD3
 - ACTA2
 - MYH11
 - MYLK

- Sprintzen-Goldberg syndrome: FBN1
- Weill-Marchesani syndrome: FBN1
- Congenital contractural arachnodycty (Beals syndrome): FBN2

- Elastine (ELN)

Ehlers-Danlos syndrome

- Type I/II (classic type): COL5A1
- Type III (hypermobility type): TNXB (MLPA analysis)
- Type IV (vascular type): COL3A1
- Type VIA (kyphoscoliotic type, recessive): PLOD1
- Type VIB (musculocontractural type): CHST14
- Type VIIa/b (arthrochalasia type, dominant): telopeptidase cleavage site in COL1A1 and COL1A2

- Osteogenesis imperfecta, dominant: type I (mild)
 - other types (II-IV) (type.....)

- COL1A1
- COL1A2

- Osteogenesis imperfecta, moderate to severe type, recessive

- CRTAP
- LEPRE1
- PPIB
- SERPINH1 (HSP47)

- Osteogenesis imperfecta with contractures (Bruck syndrome):

- PLOD2

- Porencephaly: COL4A1
- Schmid dysplasia: COL10A1

- Collagen proteins testing (**only after consultation**)
For this test are cultured fibroblasts or a skin biopsy needed

Oncogenetics

- Basal Cell Nevus (Gorlin) syndrome (PTCH1)
- Birt-Hogg-Dubé syndrome (FLCN)
- Blackfan-Diamond anemia
 - RPS19
 - RPS24
- Fanconi anemia (only after consultation, sample of the parents! should also be send)
- Peutz-Jeghers syndrome (STK11)

Neurogenetics

- Alzheimer
 - PSEN1
 - PSEN2
 - APP
- Chorea, hereditary benign (TITF1)
- Frontotemporale dementia
 - MAPT
 - PGRN
 - CHMP2B
- Parkinson disease
 - PARKIN (Park2)
 - DJ-1 (Park7)
 - PINK1 (Park6)
 - SNCA (Park1)
 - LRRK2 (Park8)

White matter disorders

- ADLD (autosomal dominant adult-onset demyelinating leukodystrophy; LMNB1)
- Hypomyelinating leukodystrophy (5, with congenital cataract; FAM126A; Hyccin)
- Pelizaeus-Merzbacher disease (PLP1)
- Pelizaeus-Merzbacher-like disease, autosomaal recessive (GJA12)

The following tests can only be requested after consulting prof. dr. M.S. van der Knaap, paediatric neeurologist (ms.vanderknaap@vumc.nl)

- Megalencephalic leukoencephalopathy with subcortical cysts (MLC1)
- Leukoencephalopathy with vanishing white matter (VWM)
- Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation (LBSL)

Developmental disorders

- BPES (Blepharophimosis, ptosis, en epicanthis inversus syndrome; FOXL2)
- Carpenter syndrome (RAB23)
- Van de Woude syndrome (IRF6)
- craniosynostosis Apert Crouzon Pfeiffer Saethre-Chotzen
 - FGFR1
 - FGFR2
 - FGFR3
 - TWIST

- Achondroplasia (FGFR3)
- Hypochondroplasia (FGFR3)
- Langer mesomelic dysplasia (SHOX)
- Thanatoforic dysplasia (FGFR3)

DNA testing, other indications

- Hyperferritinemie-cataract syndrome (FTL)
- Pulmonal arterial hypertension, idiopathic (BMPR2)
- Surfactant protein B deficiency (SFTPB)

Protein testing, other indications

- Primary Ciliary Dyskinesia / Kartageners syndrome (only after consultation, respiratory epithelial biopsy needed)



Skin biopsies

- Disinfect the skin with 70% ethanol (**do not use tincture of iodine!**), take the skin biopsies under sterile conditions, preferably from the inner side of the forearm, or during surgery from the edge of the incision.
- Place the biopsy in sterile culture medium (this can be send on request). Do not use physiological saline solutions.
- If necessary, the sample can be stored for few hours at room temperature (**not on ice**) before dispatch.

Dispatch

- Send the sample by courier, preferably at the beginning of the week (mon-wed).
- Pack the sample in such a way that breakage of the containers, and sudden changes in temperature, are prevented.
- State on the package that it is "Fragile", and that it should be stored at "room temperature".

1. Requests

- 1.1. To avoid mistakes and delays, all requests need to be submitted in a clear and unambiguous way. Use of this request form will guarantee that we will receive all data needed.
- 1.2. By accepting your request, the laboratory commits itself to perform the analysis according to the applicable quality criteria.
- 1.3. Request can be refused if they do not contain all the essential data needed to perform the testing.
- 1.4. It must be possible for the laboratory to contact the referring clinician about the requested analysis.
- 1.5. After completion of the test, an invoice will be send to the referring clinician. By sending a request, the referring clinician declares that the invoice for the analysis will be paid.
- 1.6. If applicable, European patients can use an E112 form to bill the invoice to their insurance company. This form should be attached to the request form.

2. Samples

- 2.1. All request forms should be accompanied by the required samples of the patient. The samples should be identified properly (name and dob)
- 2.2. For postnatal DNA analysis we need 2 tubes (7-10 ml) of EDTA blood (little children 2 x 3 ml), which should be stored at room temperature and send by courier.
- 2.3. For prenatal analysis we need chorionic villi, or 10 ml of amniotic fluid. For collagen diagnostics only chorionic villi can be used. Other tissues are only acceptable after consultation.
- 2.4. The laboratory can refuse all samples that do not meet the criteria outlined above.
- 2.5. The laboratory can store all samples, or the DNA extracted, for an undetermined period of time, in line with the quality procedures of the laboratory.
- 2.6. The laboratory is not responsible for treatment and storage of the sample prior to the moment it has been received by the laboratory.

3. Results

- 3.1. All results (reports, advice, information) will be delivered by the laboratory in writing.
- 3.2. Indication of the turn around times:
 - Prenatal analysis: 2-3 weeks
 - Known mutation (presymptomatic / carrier analysis / confirmation of the diagnosis): 6-8 weeks
 - Mutation scanning (analysis of an entire gene): 3-6 months.
 In case of emergency shorter turn around times can be agreed on after consultation.

4. Confidentiality

- 4.1. Confidentiality of personal details is warranted as specified in the hospital regulations of the VU University medical center.

5. Use of patient material

- 5.1. The laboratory will store all DNA samples for an undetermined period, unless the patient or the legal representatives of the patient request (in writing) to destroy the sample.
- 5.2. The laboratory uses partially anonymised samples for research purposes, but only in line with the original reason for referral. The referring clinician will only be informed about the results in case of an important finding for the patient.
- 5.3. To develop new methods and improve existing methods, the laboratory uses partially anonymised samples as controls and for validation. The laboratory request the referring clinician to inform the patient on this. In case the patient objects to this, please indicate this by ticking the appropriate box on page 1 of this form.