SYNLAB

THE FUTURE
IS HERE

Genetic diagnostics
for your daily practice

GENETIC MEDICINE is now available to EVERYONE!

EAGER TO GET STARTED? > Email us at genetics@synlab.com

MEDICAL **GENETICS**

Genetic medicine is available to everyone

It may be offered to an **individual**, **a couple**, and/or an **entire family**. Medical genetics assesses the risk of a disorder, a cancer and/or a malformation occurring or recurring.

1 > FOR INDIVIDUAL + 2 > FOR COUPLE + 3 > FOR FAMILY

*Genetic testing is one of the most **powerful tools for accurate diagnosis and treatment.***

Genetic tests are a powerful tool for diagnosis and prevention

HEREDITARY GENETIC PREDISPOSITIONS

- ✔ A family history burdened by **cancers**, especially of early onset, e.g. breast cancer and/or ovarian cancer
- ✔ The risk of developing a **genetic disorder** that is present in one's family (e.g. hemochromatosis)
- ✔ Couples or individuals concerned about **transmitting a genetic disease** to their future **children**

DELAYED OR UNCLEAR DIAGNOSIS

- ✔ Diagnosis is a major problem for many people affected by **rare diseases**:
  - Almost half have to wait more than a year for a correct diagnosis
  - 1 in 5 of these wait more than 5 years
  - 1 in 8, more than 10 years
- ✔ The use of diagnostic gene panels can shorten the diagnostic odyssey
- ✔ An appropriate diagnosis for a **previously misdiagnosed condition**

RARE AND COMMON GENETIC DEFECTS

- ✔ **Clinical signs or symptoms in a newborn**, suggestive of a possible severe monogenic disorder
- ✔ Couples who are affected by **reproductive disorders** (male or female infertility, recurrent miscarriage)

MEDICAL FUTURE, AVAILABLE TODAY

For all branches of medicine

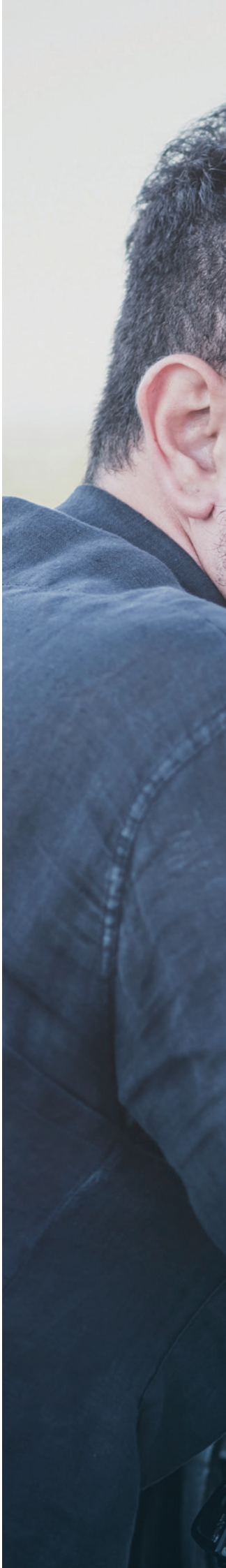
Until recently, genetic diagnostics was considered as an exotic tool for the future, reserved only for universities and research institutions. Today however, **genetic testing is firmly anchored in routine diagnostics**, both for relatively "simple" and **common conditions** *(hemochromatosis, primary lactose intolerance)* and for the **vast range of monogenic disorders**, in all branches of medicine. State-of-the-art technology, counselling and expert support are available for doctors and medical specialists all over the world.

POWER IN YOUR HANDS

Why genetic testing?

Genetic testing has become one of the most powerful tools available to healthcare providers. It provides **accurate diagnosis**, **actionable results** and **brings clarity to all medical specialties**. Genetic testing is a fundamental and routine tool for diagnosis and for identifying the most suitable treatment options for your patients and their relatives. It can:

1	DETERMINE OR EXCLUDE THE DIAGNOSIS OF A GENETIC DISORDER	e.g. Familial Mediterranean Fever *(MEFV)*
2	IDENTIFY A RARE INHERITABLE DISEASE IN A PATIENT	e.g. Ehlers-Danlos syndrome *(gene panel)*
3	PROVIDE PROGNOSTIC INFORMATION	e.g. Hereditary thrombophilia *(Factor V Leiden, Factor II)*
4	IDENTIFY HEALTHY INDIVIDUALS AT RISK OF DEVELOPING SEVERE DISEASE	e.g. Hereditary cardiac arrhythmia *(large gene panels)*
5	DETERMINE THE BEST TREATMENT AND/OR SURVEILLANCE FOR PATIENTS.	e.g. Familial pancreatic cancer *(gene panel)*
6	IDENTIFY OTHER FAMILY MEMBERS AT RISK OF DEVELOPING DISEASE	e.g. Hereditary non-polypotic colon cancer / Lynch syndrome *(gene panel)*
7	DETERMINE THE RISK OF TRANSMITTING A GENETIC DISORDER TO FUTURE CHILDREN	e.g. Fragile X syndrome *(FMR1)*
8	ENABLE REPRODUCTIVE CHOICE VIA CARRIER TESTING, PREIMPLANTATION TESTING OR PRENATAL DIAGNOSIS	e.g. Beta-thalassemia *(HBB)*



STORIES FROM OUR LABS

CASE STUDY 1 » ANY TEST

Mark (47 years of age) had **suffered from epistaxis since he was a teenager**, with cutaneous telangiectasia of the nasal mucosa. He had diffuse facial cutaneous angiomas, had a pulmonary embolism at age 40 and was **treated for arterial hypertension**. His 70-year-old mother, who had recently had a stroke, also had a long history of sporadic epistaxis.

His Internist requested **genetic testing to confirm or exclude Rendu-Osler disease** (Hereditary hemorrhagic telangiectasia, HHT). **A 4-gene panel was analysed, revealing a disease-causing variant in ACVRL1 and confirming the diagnosis of HHT type 2**. The same variant was identified in Mark's mother, in concordance with the dominant transmission of HHT2.

Based on confirmed diagnosis the family can now be followed according to International Treatment Guidelines for HHT.

STORIES FROM OUR LABS

CASE STUDY 2 » ANYWHERE

Antonia, 31 years old, was admitted to the hospital emergency department for **resuscitation after a near-death episode**. Her uncle had already died young after a similar episode. Antonia had an 8-year-old son. The cardiologist observed Antonia's tall stature and arachnodactyly and requested **NGS Panel testing for Marfan and related syndromes**.

A pathogenic variant was detected in the **FBN1 gene**, confirming the diagnosis of **autosomal dominant Marfan Syndrome** and enabling a tailored follow-up and prevention regime.

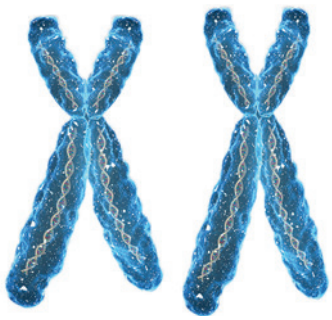
The positive result from the genetic test **provided an accurate diagnosis** and opened the way to **genetic counselling and targeted genetic testing for Antonia's son and at-risk relatives**, allowing actionable measures in a life-threatening disorder and informed reproductive choices, including the possibility of preimplantation or prenatal diagnosis.

WHAT IS **GENETIC TESTING?**

Genetic testing **helps identify or rule out specific genetic conditions**, from common to ultrarare diseases.

Genetic testing **includes chromosomal tests** such as karyotyping or microarray analysis, **biochemical tests** in particular for inborn errors of metabolism, and the current topic: **molecular genetic** (or "DNA") tests. These use multiple technologies to determine the sequence and organization of specifically targeted regions the approximately 2 % of the human genome that actually encodes genes. The specific test to be applied is selected according to the clinical context and question, whether we need to analyse one nucleotide in the whole genome (e.g. sickle-cell anemia), one gene (cystic fibrosis) or the entire exome (complex neurological syndromes). The aim is always the same: **apply the technology to provide clinicians and patents with accurate, relevant and cost-effective results and diagnostics**.

*Genetic testing can provide clinicians and patients with **accurate, relevant and cost-effective results** and diagnostics.*



A **genetic portfolio** for all medical specialties

CARDIOLOGY
DERMATOLOGY
EAR, NOSE & THROAT
ENDOCRINOLOGY
GASTROENTEROLOGY
GYNECOLOGY
HEMATOLOGY
IMMUNOLOGY
INTERNAL MEDICINE
MALFORMATIONS
METABOLIC DISORDERS
MITOCHONDRIAL DISORDERS
NEPHROLOGY
NEUROLOGY
ONCOLOGY
OPHTHALMOLOGY
PEDIATRICS
PULMONOLOGY
RHUMATOLOGY

HOW TO **GET STARTED** WITH **GENETIC TESTING**?

Expert support available all over the world

SYNLAB's genetic experts are here to support and guide health-care professionals in the complex world of medical genetic testing.

SYNLAB provides not only state-of-the-art genetic testing but also a **complete service**, from consultation and support to general practitioners and medical specialists, via genetic counselling for patients to support and follow-up for their family members. Your experience as a health-care professional matters to us, which is why we rely on our experts, counsellors and global network of laboratories to ensure a **smooth and effective process** from question to result and beyond.

EAGER TO GET STARTED?
› Email us at **genetics@synlab.com**

Genetic testing is today firmly anchored in routine diagnostics.

SYNLAB GENETIC TESTING **PROCESS**

Clinical consultation | Genetic counselling | Blood sample

CLINICIAN →

GENETIC EXPERTS

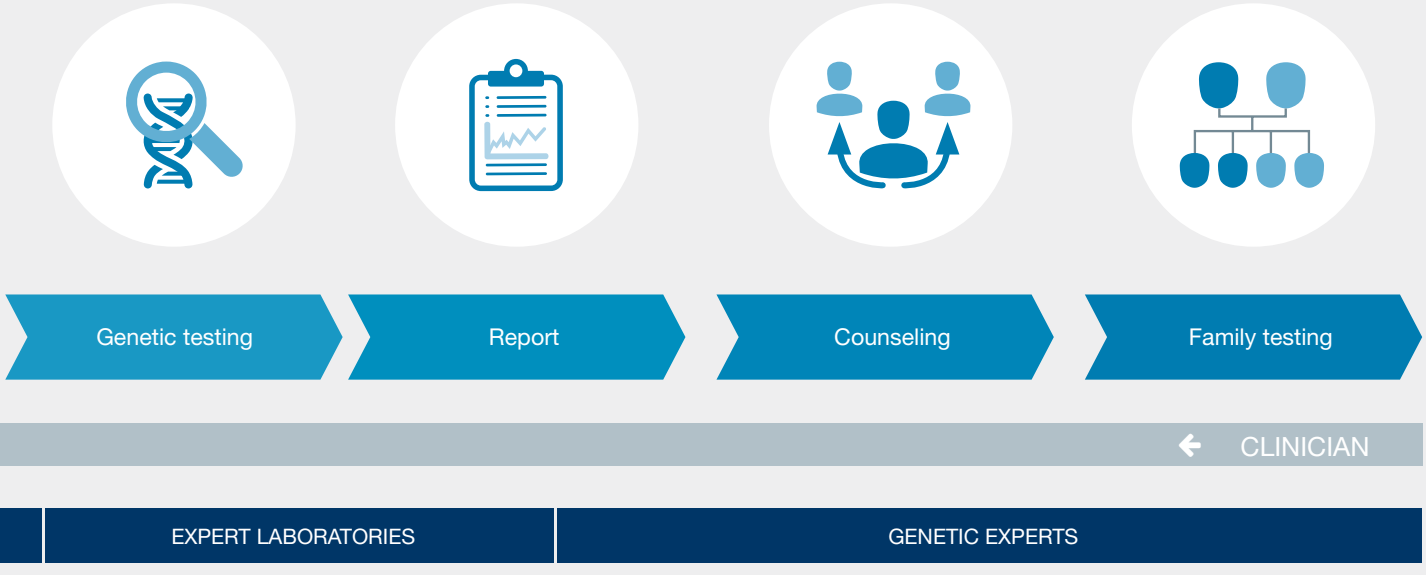
1 Pre-test genetic consultation

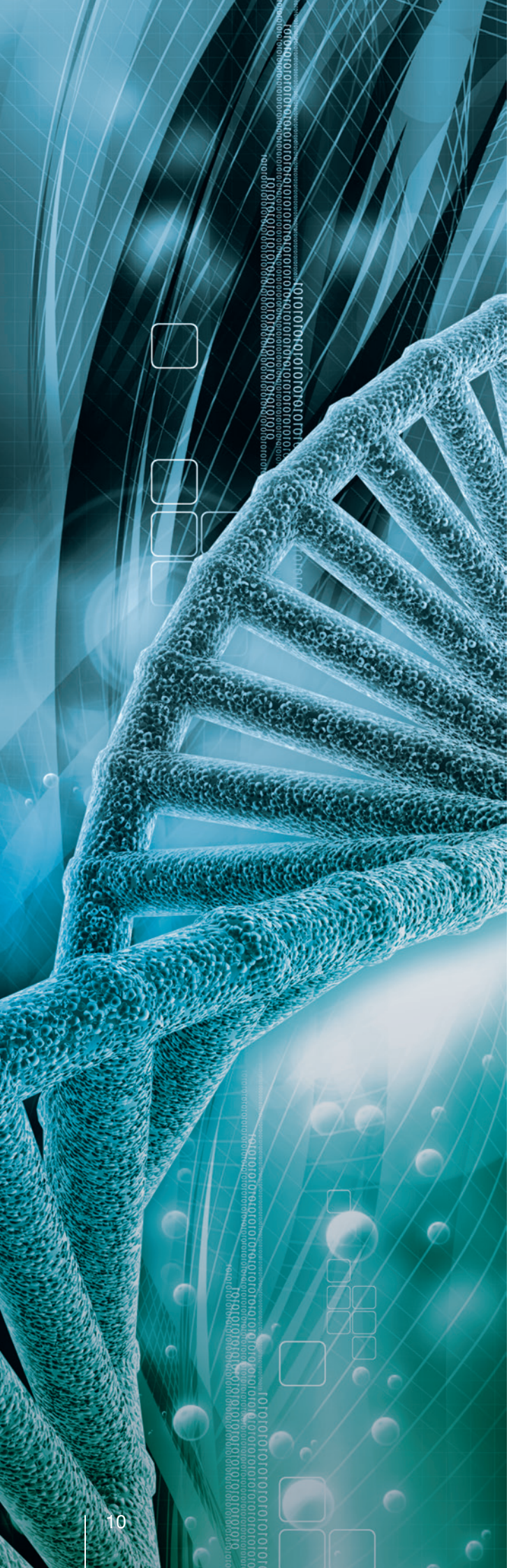
Our genetic experts and counsellors are available to **support** general practitioners, medical specialists and other health-care professionals for questions and advice **regarding genetic testing**.[1]

Genetic counselling is performed by a **trained physician** or a **specialist genetic counsellor**, generally at the request of the treating physician. During this consultation, the genetic counselling professional will **ask the patient about their personal and family history**, in order to establish the patient's exact family tree. This is the basic tool of genetic counselling, allowing the understanding of the personal and familial context, and providing important information about current or previous health conditions. It also allows him/her to ensure whether the disorder in question is **potentially genetic** or may be attributable to some other cause (environment, lifestyle, etc.). If the review of the family tree evokes a potential hereditary predisposition, and depending on the suspected pathology, the genetic counsellor may recommend carrying out a genetic test and discuss potential implications of the results for the patient, as well as for other members of his/her family. The report of this consultation, as well as any tests recommended, will be sent to the treating physician, who will decide whether or not to pursue the recommended analysis.[2]

1 May not be available in all languages or countries

2 Details may vary according to local practice and the clinician's preferences.





2 Sample collection

Our international network of laboratories, clinics and blood-collection points ensures a **fast and accessible service for** sampling **blood**, **saliva** and/or **cheek swabs** for genetic testing. After the samples are collected, they are transported to the genetic testing laboratory.

3 Genetic testing

The choice of a genetic test is critical in efficiently providing an accurate and useful result.
SYNLAB's experts can **support you in choosing the most appropriate test**, from targeted testing of a single mutation to sequencing entire exomes. In particular, current state-of-the-art next-generation sequencing (NGS) technology enables rapid and cost-effective diagnostics of rare diseases. **In many situations, genetic testing is the only solution** to avoid a diagnostic odyssey that can frequently last for years.

The majority of our SYNLAB Genetics expert laboratories work according to international **ISO 15189** accreditation standards for comprehensive quality assurance.

For **more info** about our wide range of panels and available tests in your field of expertise please contact us by e-mail.

4 Reporting

The final report not only **presents the results of the test**, but also an expert interpretation **explain the implication of the results in the context of the patient's individual situation.** Where relevant, the report may suggest further work-up or reference guidelines to help the clinician define next steps for a patient's surveillance or treatment, and also recommend appropriate familial follow-up.

5 Post-test genetic counselling

After receiving the results of a genetic analysis, our geneticists can provide **clear explanations about the genetic aspects to the treating physician**, the patient, and/or other members of the family. The genetic experts and counsellors have the role of **supporting the treating physician** and the post-test consultations typically follow one of two common scenarios:

EITHER The doctor **refers the patient/couple to a genetic counsellor**, for an explanation of the genetic implications, for themselves and for other members of their families. The counsellor may recommend testing for people who appear to be at risk.

OR The **genetic expert or counsellor discusses with the referring doctor**, to provide support on the interpretation of the report and the recommended next genetics steps.

STORIES FROM OUR LABS

CASE STUDY 3 » ANYTIME

Eight weeks into their first pregnancy, Piotr and Katerina informed their gynecologist that **Piotr's brother had died shortly after birth with Smith-Lemli-Opitz syndrome** (SLOS), a genetic disease which associates congenital malformations, growth retardation and intellectual deficit. Assuming the diagnosis was accurate (it had **never been confirmed by molecular testing**), there was a **risk of about 1/600** that the child be affected. This risk was not acceptable to the couple and they requested prenatal diagnosis and/or genetic testing.

The geneticist explained that a biochemical test could be used for prenatal diagnosis in each pregnancy, but that genetic testing could determine once and for all if the couple was at risk. Piotr requested sequencing of the causative **DHCR7 gene and the normal result indicated that the risk of having a child with SLOS was extremely low (1/20'000**).

WHAT TYPE OF **GENETIC TEST** TO CHOOSE?

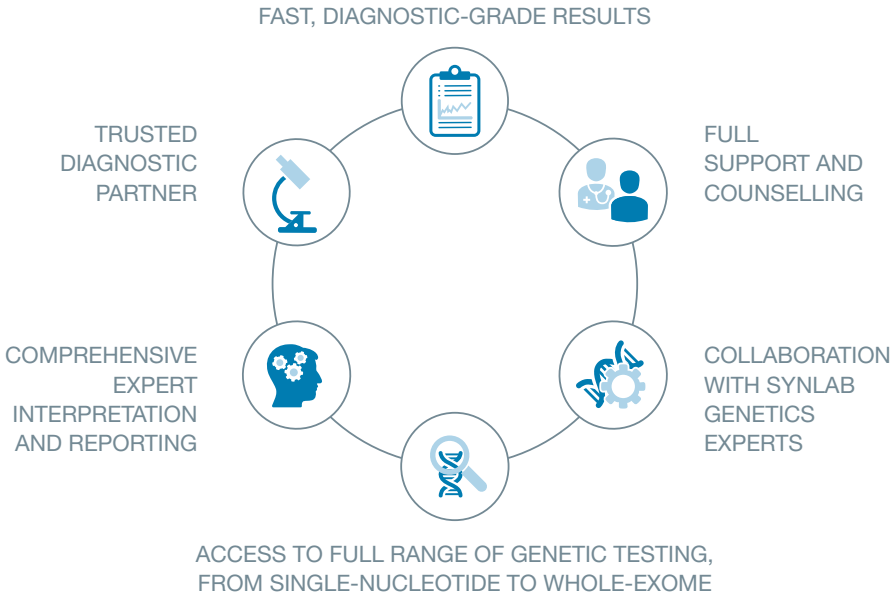
A complete array of genetic tests

SYNLAB offers a **complete array of genetic tests** to ensure that you **receive the diagnostic support you need**, and your patients the answers they seek – regardless of the situation. Our genetic experts are **available to support** you in the choice of the most appropriate test or even to develop personalized panels for your patient.

	WHEN?	EXAMPLES
TARGETED VARIANT	• Diagnostic or carrier testing of common or known founder variants. • Confirmation of results from a research or direct-to-consumer ("internet testing") laboratory. • Preparation for preimplantation or prenatal testing.	• Three BRCA1/2 variants common in Ashkenazi Jews. • AIRE founder mutation in Finnish patients with APECED. • Rare NDRG1 neuropathy variant highly prevalent in Roma Gypsies.
SINGLE-GENE	• Diagnostic confirmation of a strong suspicion of a specific genetic disorder. • Carrier testing for a couple where one partner is a known carrier of a variant in a particular gene.	• Recurrent febrile episodes with abdominal pain, arthritis, inflammation: MEFV sequencing for familial Mediterranean fever. • Male carrier of a cystic fibrosis-causing variant; his partner requests CFTR testing to determine their risk of having an affected child.
PANEL	• Diagnostic clarification: Your patient has a known or suspected clinical diagnosis and the causative genes are well-described and available in one of our gene panels.	• Patient with thoracic aortic aneurysm and a suggestive family history: aorta panel of 52 genes associated with syndromic and isolated forms.
WHOLE EXOME SEQUENCING (WES)	Your undiagnosed patient has some of the following: • A complex phenotype with multiple differential diagnoses. • A genetically heterogeneous disorder. • A suspected genetic disorder but specific genetic testing is not available. • When previous genetic testing has not clarified the diagnosis.	• WES is progressively recommended as a first-line diagnostic in cases of rare disease without a clear differential diagnosis, to accelerate and facilitate personalized medical care. • WES can be performed on the index patient alone, but we recommend testing "trios" including both parents, to improve variant characterization and interpretation.
PREIMPLANTA-TION OR PRENATAL DIAGNOSIS	Couple at high risk of transmitting a severe genetic disorder to their offspring: • After having an affected child. • Based on family history. • After positive carrier screening.	• Couple who lost their first child with spinal muscular atrophy (SMA, SMN1). • Couple found to be carriers of Tay-Sachs disease (HEXA) after expanded carrier screening.

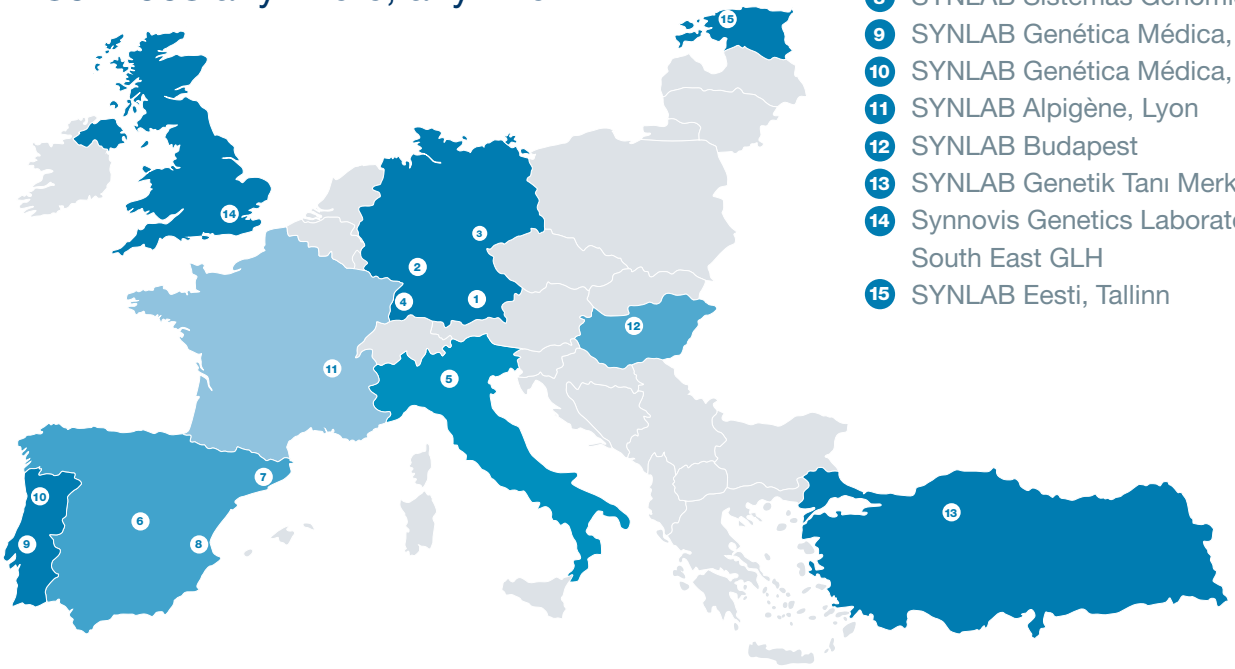
WHY CHOOSE US?

Cutting-edge genetics technology and medical expertise blended with comprehensive reporting and support



WIDE NETWORK OF EXPERT LABS

We provide you with **fast, reliable actionable genetic diagnostic services** anywhere, anytime



1. SYNLAB MVZ Humangenetik München
2. SYNLAB MVZ Humangenetik Mannheim
3. SYNLAB Oncoscreen Jena
4. SYNLAB MVZ Humangenetik Freiburg
5. SYNLAB Italia, Castenedolo
6. SYNLAB Madrid
7. SYNLAB Barcelona
8. SYNLAB Sistemas Genomicos, Valencia
9. SYNLAB Genética Médica, Lisbon
10. SYNLAB Genética Médica, Porto
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12. SYNLAB Budapest
13. SYNLAB Genetik Tanı Merkezi, Ankara
14. Synnovis Genetics Laboratory, London South East GLH
15. SYNLAB Eesti, Tallinn

About SYNLAB Group

SYNLAB Group is the leading medical diagnostic services provider in Europe. SYNLAB offers a full range of innovative and reliable medical diagnostics for patients, practising doctors, clinics and the pharmaceutical industry.

Providing the leading level of service within the industry, SYNLAB is the partner of choice for healthcare professionals. SYNLAB's services also encompass veterinary and environmental laboratory analysis.

SYNLAB operates in 33 countries across four continents and holds leading positions in most markets. Over 27,000 employees contribute every day to the Group's world-wide success.

SYNLAB carries out 600 million laboratory tests per year, achieving sales revenues of more than EUR 2.6 billion.

More information can be found on **www.synlab.com**

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