MOLECULAR HEALTH

Transforming biomedical data
into actionable insights
molecularhealth.com

Impressively reliable and rapid

The hereditary disease diagnostics of the future

GUIDE/MENDEL

This might interest you:

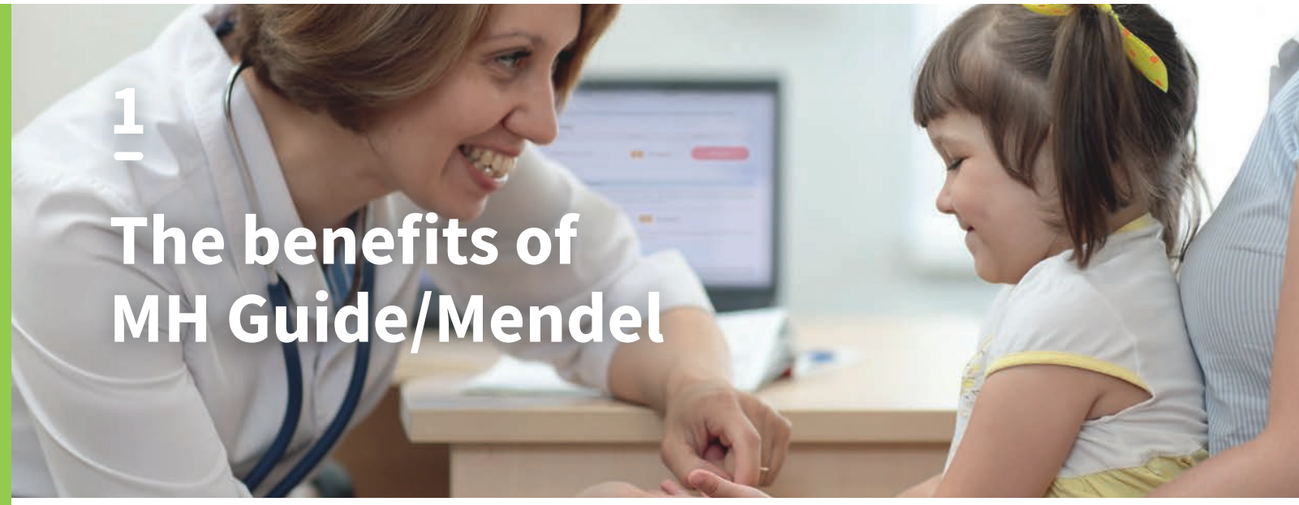
1 The benefits of MH Guide/Mendel

2 The MH Guide/Mendel process

3 Integration in lab workflows

4 Generate the report: just a few, intuitive steps

5 How to reach Molecular Health



1

The benefits of MH Guide/Mendel

Fast, precise evaluation of germline variants

MH Guide/Mendel is optimized for evaluating germline variants associated with hereditary diseases. The software application is a module of MH Guide and supports human genetics laboratories in next-generation sequencing (NGS)-based assessment of germline variants.

How human genetics laboratories benefit from MH Guide/Mendel:

- **Approved for diagnostic use**
  MH Guide/Mendel is a module of MH Guide, which is approved as an IVD medical device according to the EU regulation 2017/746 (IVDR).
- **Faster results**
  By automatically accessing relevant databases and pre-classifying variants according to ACMG criteria, MH Guide/Mendel quickly and accurately identifies and annotates gene variants associated with hereditary diseases.
- **Easy to integrate**
  Flexible interfaces make it possible to analyze standard data formats from the sequencing of commercially-available or proprietary gene panels, independent of the platform used.
- **Customizable evaluation**
  The filtering and editing options within the software allow quick access to the most important information. Users can store their own variant classifications in the protected area of their account.
- **Scalable analysis process**
  MH Guide/Mendel's optimized workflow allows a high sample throughput.
- **Audited quality**
  Molecular Health Molecular Health's quality management system (QMS) is certified according to EN ISO 13485, for the design and manufacture of medical devices. Users benefit from the safety and reliability of MH software applications.

2

The MH Guide/Mendel process

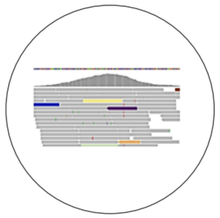
Use global knowledge to reliably aid in the diagnosis of hereditary diseases or disease predispositions

MH Guide/Mendel identifies and classifies variants for hereditary diseases. The software automatically matches these with data based on the comprehensive, regularly updated, and quality controlled Dataome database. This contains, among other things, the currently published biomedical knowledge on relevant hereditary diseases and pathogenic gene variants.

You can use any commercial or proprietary gene panel and have the data analyzed in VCF format with MH Guide/Mendel.

MH Guide/Mendel summarizes all of the relevant results in individual reports that provide users with clear, specific information on genetic mutations associated with hereditary diseases.

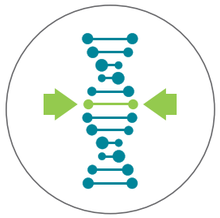
Genomic data from a blood sample



Technology-independent data upload

- VCF files
- Commercial panels
- Custom panels

Interpretation of genetic variants



Automated database comparison and classification

- Public databases
- MH database
- ACMG classification
  Richards S et al., Genet Med 2015
- Automated CVI variant narratives

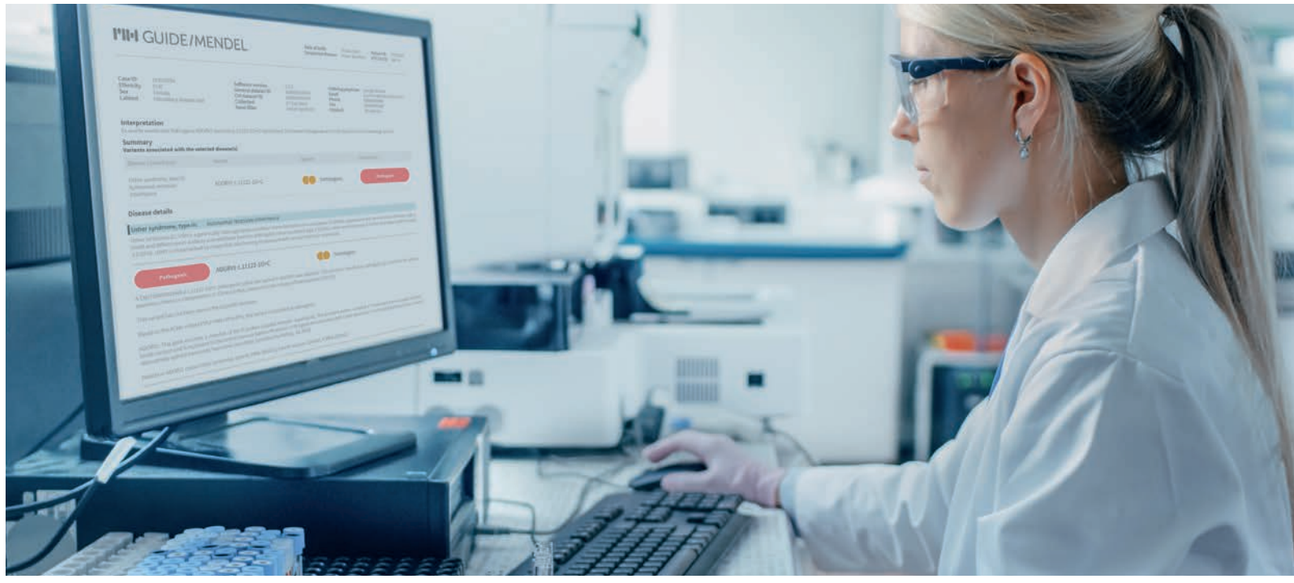
MH Guide/Mendel report

Standardized, customizable report

- Your individual summary
- Variant classification
- Functional effects

3

Integration in lab workflows



Flexibility and data security in one

The web-based software application can be easily integrated in the laboratory. It enables the annotation and interpretation of genetic variants from common NGS or other analysis platforms.

Approved for clinical use
MH Guide/Mendel is a module of MH Guide, a software application approved in Europe as an IVD medical device according to the EU regulation 2017/746 (IVDR).

SaaS – individually scalable
MH Guide/Mendel is offered as scalable SaaS (Software as a Service) to suit small and large institutions alike.

Customizable patient reports
The design, content, and format of analysis reports can be adapted to individual needs on request.

Flexible input and output formats
Our applications process the standard data format VCF. Output formats are PDF, and JSON. Structured export of variant information is available in CSV format for single and multi case analysis.

Secure data transmission
MH Guide/Mendel provides secure transmission of patient data through advanced encryption standards (SSL/TLS, AES-256) and storage of patient data with controlled access authorization.

Data center architecture
Molecular Health utilizes data centers certified according to international security standards, including Trusted Site Infrastructure (TSI) and ISO 27001. Molecular Health performs third-party penetration tests and maintains a continuous process for vulnerability scanning and handling.

Guaranteed security of patient data
MH Guide meets the requirements of:

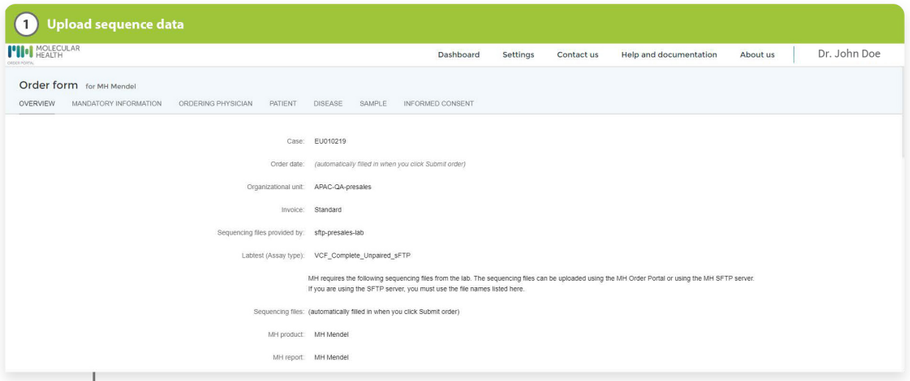
- General Data Protection Regulation (GDPR) in Europe.
- Health Insurance Portability and Accountability Act (HIPAA) in the USA.
- Genetic Diagnostics Act (GenDG) in Germany.

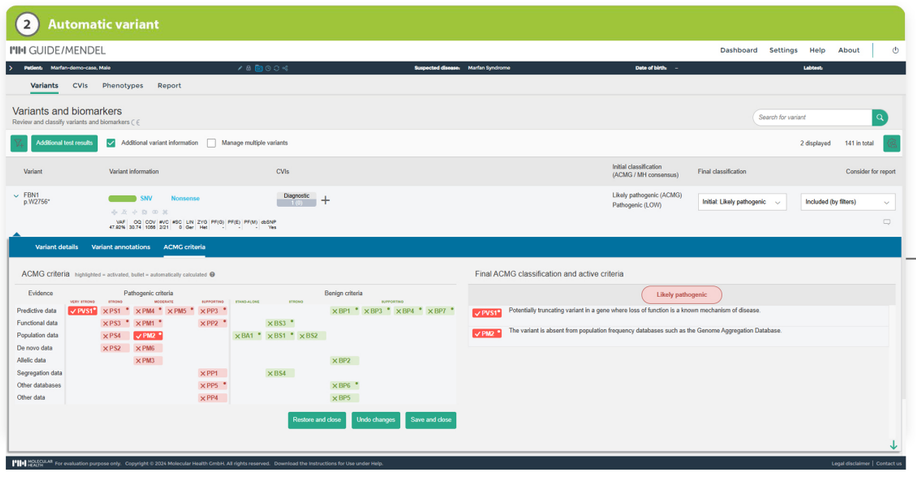
Efficient workflows in your lab
MH Guide/Mendel lets you optimize your everyday processes. The cloud-based software automates the interpretation of germline variants and delivers high-quality analyses.

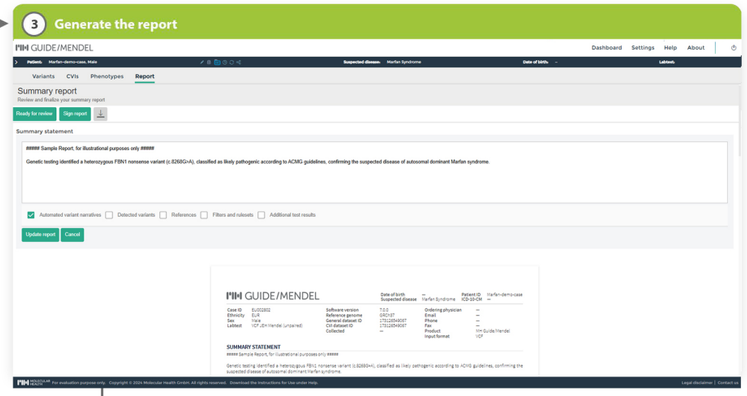
4

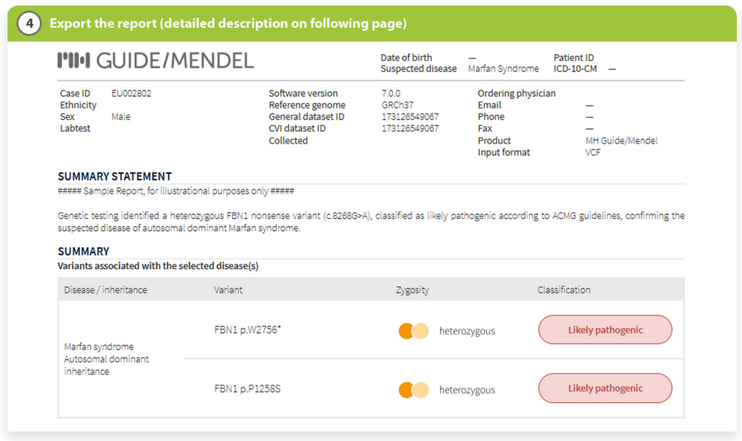
Generate the report: just a few, intuitive steps

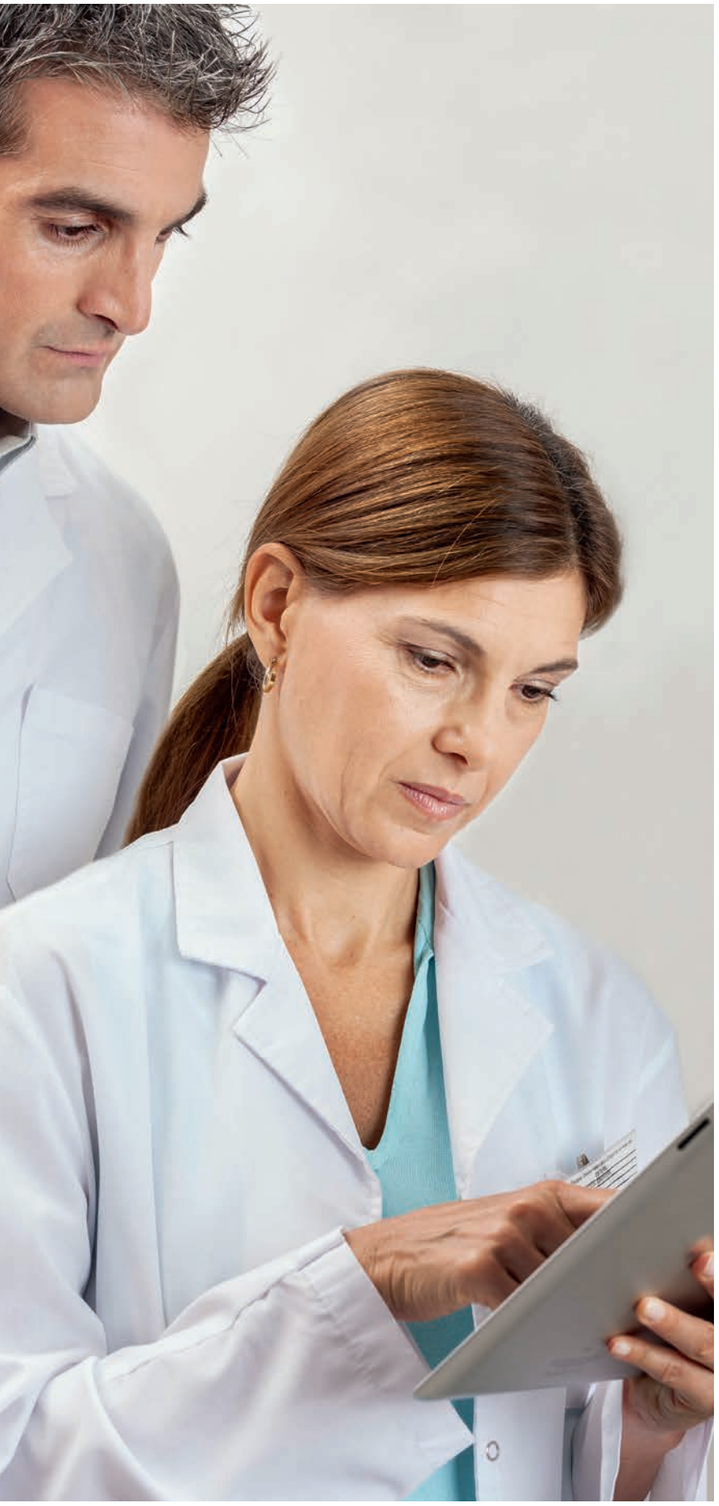
How it looks on your screen: from raw data upload to final patient report











Everything at a glance:

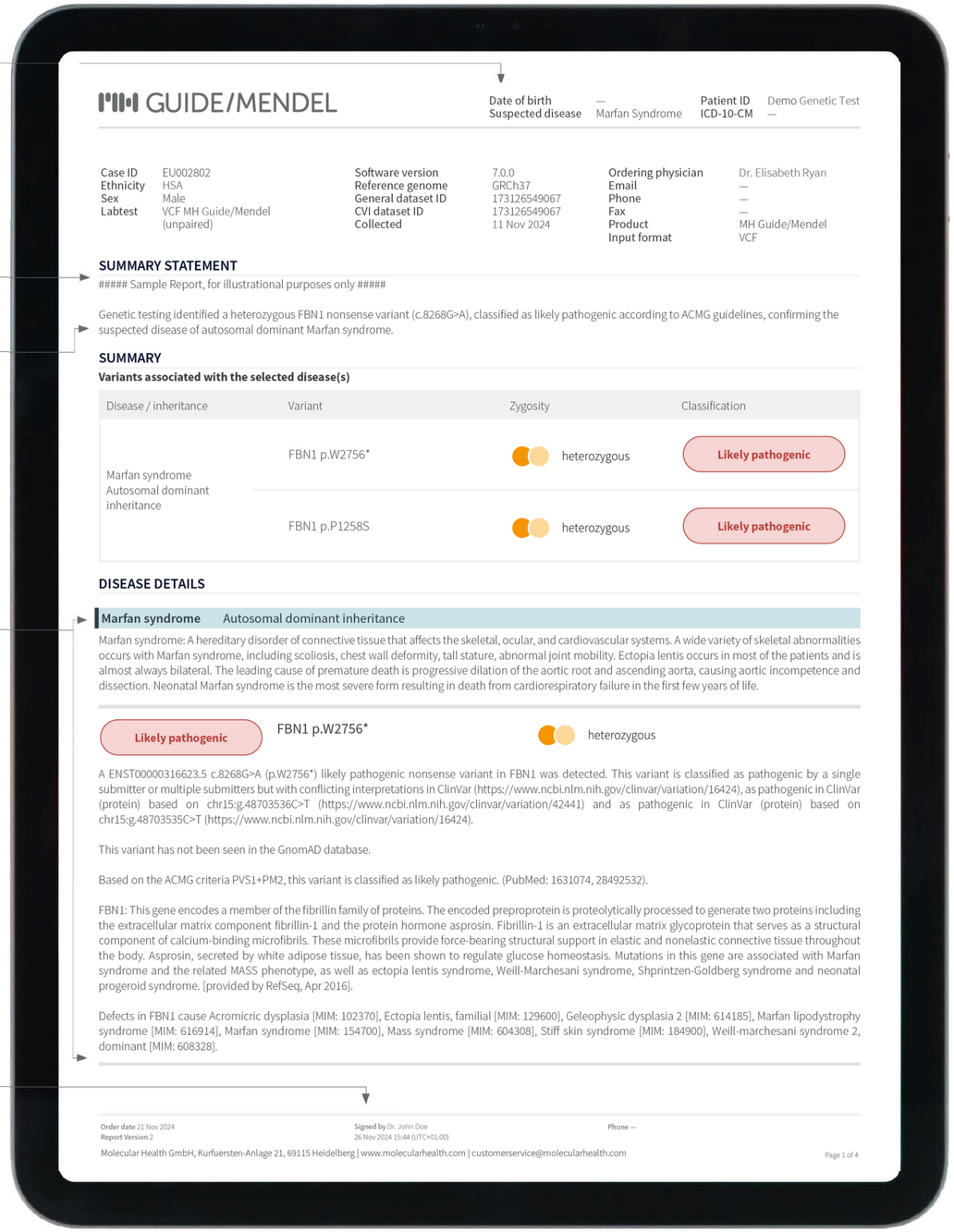
Patient data and suspected diagnosis

Your interpretation of findings and comments for colleagues and patients

Overview of detected variants and phenotype, including zygosity and classification

Detailed information on the disease, mode of inheritance, information on the source of genotype-phenotype correlation, and PubMed references

Electronic signature of the human geneticist in charge



GUIDE/MENDEL

Date of birth —
Suspected disease Marfan Syndrome
Patient ID Demo Genetic Test
ICD-10-CM —

Case ID	EU002802	Software version	7.0.0	Ordering physician	Dr. Elisabeth Ryan
Ethnicity	HSA	Reference genome	GRCh37	Email	—
Sex	Male	General dataset ID	173126549067	Phone	—
Labtest	VCF MH Guide/Mendel (unpaired)	CVI dataset ID	173126549067	Fax	—
		Collected	11 Nov 2024	Product	MH Guide/Mendel
				Input format	VCF

SUMMARY STATEMENT

Sample Report, for illustrational purposes only

Genetic testing identified a heterozygous FBN1 nonsense variant (c.8268G>A), classified as likely pathogenic according to ACMG guidelines, confirming the suspected disease of autosomal dominant Marfan syndrome.

SUMMARY

Variants associated with the selected disease(s)

Disease / inheritance	Variant	Zygosity	Classification
Marfan syndrome Autosomal dominant inheritance	FBN1 p.W2756*	heterozygous	Likely pathogenic
	FBN1 p.P1258S	heterozygous	Likely pathogenic

DISEASE DETAILS

Marfan syndrome Autosomal dominant inheritance

Marfan syndrome: A hereditary disorder of connective tissue that affects the skeletal, ocular, and cardiovascular systems. A wide variety of skeletal abnormalities occurs with Marfan syndrome, including scoliosis, chest wall deformity, tall stature, abnormal joint mobility. Ectopia lentis occurs in most of the patients and is almost always bilateral. The leading cause of premature death is progressive dilation of the aortic root and ascending aorta, causing aortic incompetence and dissection. Neonatal Marfan syndrome is the most severe form resulting in death from cardiorespiratory failure in the first few years of life.

Likely pathogenic FBN1 p.W2756* heterozygous

A ENST00000316623.5 c.8268G>A (p.W2756*) likely pathogenic nonsense variant in FBN1 was detected. This variant is classified as pathogenic by a single submitter or multiple submitters but with conflicting interpretations in ClinVar (https://www.ncbi.nlm.nih.gov/clinvar/variation/16424), as pathogenic in ClinVar (protein) based on chr15:g.48703536C>T (https://www.ncbi.nlm.nih.gov/clinvar/variation/42441) and as pathogenic in ClinVar (protein) based on chr15:g.48703535C>T (https://www.ncbi.nlm.nih.gov/clinvar/variation/16424).

This variant has not been seen in the GnomAD database.

Based on the ACMG criteria PVS1+PM2, this variant is classified as likely pathogenic. (PubMed: 1631074, 28492532).

FBN1: This gene encodes a member of the fibrillin family of proteins. The encoded preproprotein is proteolytically processed to generate two proteins including the extracellular matrix component fibrillin-1 and the protein hormone asprosin. Fibrillin-1 is an extracellular matrix glycoprotein that serves as a structural component of calcium-binding microfibrils. These microfibrils provide force-bearing structural support in elastic and nonelastic connective tissue throughout the body. Asprosin, secreted by white adipose tissue, has been shown to regulate glucose homeostasis. Mutations in this gene are associated with Marfan syndrome and the related MASS phenotype, as well as ectopia lentis syndrome, Weill-Marchesani syndrome, Shprintzen-Goldberg syndrome and neonatal progeroid syndrome. [provided by RefSeq, Apr 2016].

Defects in FBN1 cause Acromicric dysplasia [MIM: 102370], Ectopia lentis, familial [MIM: 129600], Geleophysic dysplasia 2 [MIM: 614185], Marfan lipodystrophy syndrome [MIM: 616914], Marfan syndrome [MIM: 154700], Mass syndrome [MIM: 604308], Stiff skin syndrome [MIM: 184900], Weill-marchesani syndrome 2, dominant [MIM: 608328].

Order date 21 Nov 2024
Report Version 2
Signed by Dr. John Doe
26 Nov 2024 15:44 (UTC+01:00)
Phone —

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How to reach Molecular Health

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We develop and deliver innovative technologies for in silico medicine and precision medicine

Our solutions enable the conversion of large amounts of data into evidence-based, medically relevant results for the actors in the healthcare sector. Therewith, we provide molecular pathologists, geneticists, physicians, and patients with better information on diagnoses and therapy options. We support pharmaceutical and health organizations by optimizing clinical studies in the development of promising active ingredients and meaningful disease models.