CENTOGENE
THE RARE DISEASE COMPANY

IDS Factsheet

Mucopolysaccharidosis Type 2 (MPS II)

CENTOGENE ID	140
Gene(s) name (OMIM®, HGNC)	*IDS*
Gene OMIM®	300823
Disease OMIM®	309900
Gene location	Xq28

INHERITANCE PATTERN
X-linked recessive

DISEASE SYNONYMS
Mucopolysaccharidosis Type 2 (MPS II), MPS2, Iduronate 2-Sulfatase Deficiency, *IDS* Deficiency, Sulfoiduronate Sulfatase Deficiency, SIDS Deficiency, Hunter Syndrome

MATERIAL

Minimum DNA (µg)	Minimum EDTA Blood (ml)	Minimum Filtercards (pcs)
2	1	1

TURNAROUND TIME
Estimated working days upon sample receipt

Enzyme (Iduronate-2-sulfatase)	Full Gene Sequencing	DEL / DUP Analysis
7	15	15

We recommend ordering parallel or reflex testing workflows to shorten the total turnaround time.

Pathophysiology

Mucopolysaccharidosis type II (also known as Hunter syndrome) is caused by mutations in the IDS gene.[1] Genetic defects lead to a lack or deficiency of Iduronate-2-sulfatase. To date, more than 730 variants have been reported in this gene.

MPS II mainly affects males; however, heterozygous females with very mild symptoms have also been reported. The estimated incidence of MPS II is between 1:100,000 and 1:170,000 of male births.[2]

Clinical Features

According to the severity of symptoms, MPS II is divided into two groups: (1) MPS IIA; (2) MPS IIB.[3] Patients affected with MPS IIA start to present symptoms earlier in life between the ages of 2 and 4. Patients show progressive cognitive decline, with their life expectancy between the ages of 10 and 15 years old. With MPS IIB, patients manifest slow progression of disease, experience normal intellectual development, and show different life expectancy. MPS II has multisystem involvement, and the rate of progression related to the central nervous system (CNS) is the most significant feature of MPS II.

The major clinical features of MPS II include the following:[4,5]

- Coarse facial features
- Short stature with dysostosis multiplex and short neck
- Obstructive airway and respiratory complications
- Macrocephaly with or without communicating hydrocephalus
- Retinal degeneration without corneal clouding
- Conductive and sensorineural hearing loss
- Enlarged adenoids often requiring adenectomy
- Frequent inguinal / umbilical hernia
- Hepatosplenomegaly
- Frequent ear / sinus infections

Differential Diagnosis

The differential diagnosis of MPS II includes all of the other MPS disorders, given the significant overlap of clinical presentation and radiologic findings. Additional diseases such as multiple sulfatase deficiency, mucolipidosis types II and III, Spondyloepiphyseal dysplasia and Legg-Calve-Perthes disease may present with findings similar to MPS II.[6]

Diagnostic Strategy: Biochemistry & Genetics

To establish the diagnosis, CENTOGENE offers an enzymatic activity assay (Quantification of Iduronate 2-sulfatase) followed by molecular genetic testing (full gene sequencing and deletion/duplication analysis of the *IDS* gene). We also offer a broad selection of Next Generation Sequencing (NGS) panels which are designed for the molecular diagnostics of related conditions/phenotypes.

Biochemistry

- Iduronate 2-sulfatase (enzyme) fluorimetry-based activity testing

Genetics

- *IDS* sequencing covering the entire coding region, exon/intron boundaries, and 200 bp of the gene promoter (single gene or panel testing). Copy Number Variant (CNV) analysis derived from NGS data is also included
- If no pathogenic or likely pathogenic variants are found, *IDS* deletion/duplication analysis is recommended to detect large gene rearrangements that cannot be detected via sequencing

For differential diagnosis, we recommend CentoMetabolic MOx (comprehensive coverage with more than 200 genes and biochemical testing) or Whole Genome Sequencing (WGS) covering those genes which are either implicated in an overlapping phenotype or could be involved in a similar pathway but are not strongly clinically implicated based on current literature.

Treatment

Many complications can be avoided with a timely diagnosis and early treatment implementation. Enzyme replacement therapy (ERT) with Idursulfase and Hematopoietic stem cell transplantation are available therapeutic options. However, ERT does not improve neurocognitive function because of its inability to cross the blood-brain barrier.

Referral Reasons

The following individuals are candidates for this *IDS* gene testing:

- Individuals with a family history of MPS II and presentation of the most common symptoms, such as severe airway obstruction, skeletal deformities, cardiomyopathy, and neurologic decline
- Individuals without a positive family history, but with symptoms resembling MPS II
- Individuals with a negative but suspected family history, in order to perform proper genetic counseling (prenatal analyses are recommended in families with affected individuals)

Test Utility

Sequencing as well as deletion/duplication analysis of the *IDS* gene and related genes should be performed in all individuals suspected of having MPS II. In parallel, other genes reported as related to this clinical phenotype should also be analyzed for the presence of variants due to the overlap in many clinical features caused by those particular genes.

Confirmation of a clinical diagnosis of MPS II through enzymatic and molecular testing can allow for genetic counseling and direct medical management. Genetic counseling can provide a patient and/or family with the natural history of MPS II, identify at-risk family members, provide information on reproductive risks as well as preconception/prenatal options, and allow for appropriate referral for patient support and/or resources.

1 Zhou J et al. Intractable & Rare Research. 2020; 9;1-9
2 Froissart et al. Cli Genet. 1998; 53: 362
3 Neufeld & Muenzer. In: Scriver et al. The Metabolic and Molecular Bases of Inherited Disease. 2001: 3430
4 Nelson Textbook of Pediatrics. Edition 21. Philadelphia, PA: Elsevier, 2020; chapter 107
5 Fenton & Rogers. Mucopolysaccharidosis type II. eMedicine Journal [serial online]. 2006
6 Scarpa M. Mucopolysaccharidosis Type II. 2007 Nov 6 [Updated 2018 Oct 4]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021. Available from: www.ncbi.nlm.nih.gov/books/NBK1274/