Specific information Diabetes

(Version January 2026)

Website links:

Amount of patient material to submit
Turnaround times mutational scanning and prices

Monogene diabetes

OMIM: Maturity Onset Diabetes of the Young (MODY), Renal cysts and diabetes syndrome (RCAD), Permanent Neonatal Diabetes Mellitus (PNDM), Persistent hyperinsulinemic hypoglycaemia, Hyperproinsulinism, Insulin dependent diabetes.

As of October 1, 2015, gene panel analysis is offered for MODY with NGS (**22 genes**, **core genes**: HNF4A (NM_175914.4), GCK (NM_000162.5), HNF1A (NM_000545.4), HNF1B (NM_000458.2); **non-core genes**: PDX1 (NM_000209.4), NEUROD1 (NM_002500.4), CEL (NM_001807.4), INS (NM_000207.2), ABCC8 (NM_000352.3), KCNJ11 (NM_000525.3), GATA6 (NM_005257.4), WFS1 (NM_006005.3), CISD2 (NM_001008388.5), GATA4 (NM_002052.4), PAX6 (NM_001604.3), PCBD1 (NM_000281.3) RFX6 (NM_173560.4), ZFP57 (NM_001109809.3), LMNA (NM_170707.3), PPARG (NM_015869.4), PLIN1 (NM_002666.5), INSR (NM_000208.3).

Genes/conditions that can be requested separately (i.e. not as part of the gene panel)

OMIM	**Disorder/Referral reason**	**Gene**
125850	Maturity Onset Diabetes of the Young type 1	*HNF4A*
125851	Maturity Onset Diabetes of the Young type 2; Permanente Neonatale Diabetes Mellitus (PNDM), Persisterende hyperinsulinemische hypoglykemie	*GCK*
600496	Maturity Onset Diabetes of the Young type 3	*HNF1A*
606392, 260370	Maturity Onset Diabetes of the Young type 4, Pancreatic agenesis	*PDX1 (IPF1)*
137920	Renal cysts and diabetes syndrome (RCAD); former Maturity Onset Diabetes of the Young type 5	*HNF1B*
606394	Maturity Onset Diabetes of the Young type 6	*NEUROD1*
613370, 125852, 606176,616214	Maturity Onset Diabetes of the Young 10 (no OMIM nr), Permanent Neonatal Diabetes Mellitus (PNDM), Hyperproinsulinemic, Insulin dependant diabetes	*INS*
616329, 610582,601820	Maturity Onset Diabetes of the Young 13, Permanent Neonatal Diabetes Mellitus (PNDM), Transient neonatal Diabetes mellitus type 3, Familial Hyperinsulinemic hypoglycaemia type 2,	*KCNJ11*

Gene	Method
HNF4A	Sequence analysis of the entire coding region (exon 2 to 10) including promoter region and intron/exon junctions
GCK	Sequence analysis of the entire coding region (exon 1A to 10) including intron/exon junctions
HNF1A	Sequence analysis of the entire coding region (exon 1 to 10) including promoter region and intron/exon junctions
PDX1 (IPF1)	Sequence analysis of the entire coding region (exon 1 and 2) including intron/exon junctions and MLPA of exon 1 and 2 (MRC Holland kit P357)
HNF1B	Sequence analysis of the entire coding region (exon 1 to 9) including promoter region and intron/exon junctions and MLPA exon 1 to 9 HNF1B (MRC-Holland kit P241-D1)
NEUROD1	Sequence analysis of the entire coding region (exon 1 and 2) including intron/exon junctions and MLPA of exon 1 and 2 (MRC Holland kit P357)
INS	Sequence analysis of the entire coding region (exon 1 and 2) including intron/exon junctions and MLPA of exon 1 and 2 (MRC Holland kit P357)
KCNJ11	Sequence analysis of the entire coding region (exon 1)

Procedure:

• If material is submitted with referral reason confirmation/exclusion of MODY or analysis of three or more genes, the MODY gene panel is used by default. SNV analysis and CNV analysis are always combined. If CNV analysis fails, MLPA can be considered.

• In the case of known mutations, only the pathogenic mutation occurring in the family is examined with Sanger sequencing or MLPA.

• Analysis of the *HNF1B* gene is used if kidney abnormalities are also suspected (Renal cysts and diabetes (RCAD) syndrome; formerly also called MODY5). Because approximately 50% of these patients have a deletion of the entire gene, CNV and SNV analysis are performed. In the majority of patients with an *HNF1B* deletion, the deletion is larger than the *HNF1B* gene; CNV analysis is used to determine the size of the deletion.

Detection ratio:

HNF1A: 29,1%; GCK: 23,5%; *HNF4A*: 10,2%; the rest are very rare except for *HNF1B*.
Not changed when analyzing MODY gene panel.

Gen	Gene product	Locus	Inheritance	OMIM number	Reference sequence
HNF4A	HNF4A	20q12-q13.1	Autosomal dominant	600281	NC_000020.9, NM_175914.3
GCK	GCK	7p15-p13	Autosomal dominant	138079	NC_000007.12; NM_000162.3
HNF1A	HNF1A	12q24.2	Autosomal dominant	142410	NC_000012.10; NM_000545.4
PDX1 (IPF1)	PDX1 (IPF1)	13q12.1	Autosomal dominant	600733	NC_000013.10; NM_000209.3
HNF1B	HNF1B	17q12	Autosomal dominant	189907	NC_000017.10, NM_000458.2
NEUROD1	NEUROD1	2q32	Autosomal dominant	601724	NM_002500.2
INS	INS		Autosomal dominant		NG_007114.1; NM_000207.2
KCNJ11	KCNJ11	11p15.1	Autosomal dominant	600937	NM_000525.3

Databases / links:
All genes: HGMD: http://www.biobase-international.com/product/hgmd
GCK, *HNF1A* and *HNF4A*: LOVD: http://grenada.lumc.nl/LOVD2/diabetes/home.php

For the genes in the gene panel, see gene panels on the website.

MIDD (Maternally Inherited Diabetes and Deafness)

Specific information Maternally inherited diabetes and Deafness syndrome (MIDD)

OMIM: 520000

Gene	Method
MT-TL1, tRNA-leu (UUR)	Detection of the m.3243A>G point mutation using PCR, restriction enzyme analysis (ApaI) and fragment electrophoresis (heteroplasmy level of 1% is easily detectable)

Procedure:

This method determines whether this mitochondrial mutation is present in a small percentage (1-2%) of cells. Family members can then be referred for confirmation/exclusion of the diagnosis. This same mutation is responsible for the much more severe MELAS syndrome; requests for MELAS are submitted elsewhere.

Detection ratio: to be determined.

Gene	Gene product	Locus	Inheritance	OMIM number	Reference sequence
MT-TL1	MTTL1	mitochondrial	maternal	590050	NC_012920.1