THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

Pancreatic Agenesis Testing: Mutation Analysis of *PDX1*

Clinical Features

Pancreatic Agenesis [OMIM#260370] is characterized by early onset insulin-dependent diabetes and pancreatic exocrine insufficiency.

Molecular Genetics

Homozygous mutations in the *PDX1* [OMIM#600733] gene leads to neonatal diabetes, which has been attributed to pancreatic agenesis, while heterozygous mutations in *PDX1* result in a MODY4 [OMIM#606392] phenotype (1, 2). As MODY may be largely asymptomatic disease in younger years, hyperglycemia in obligate carriers may exist for years to decades before a diagnosis is made.

Inheritance

Pancreatic agenesis is a rare disorder. *PDX1* mutations follow an autosomal recessive inheritance pattern. Parents of an affected child are most likely obligate carriers. Recurrence risk for carrier parents is 25%.

Test methods:

Comprehensive sequence coverage of the *PDX1* gene is performed. Targets of interests are enriched and prepared for sequencing using the Agilent SureSelect system. Sequencing is performed using Illumina technology and reads are aligned to the reference sequence. Variants are identified and evaluated using a custom collection of bioinformatic tools and comprehensively interpreted by our team of directors and genetic counselors. All pathogenic and likely pathogenic variants are confirmed by Sanger sequencing. The technical sensitivity of this test is estimated to be >99% for single nucleotide changes and insertions and deletions of less than 20 bp. Our CNV detection algorithm was developed and its performance determined for the sole purpose of identifying deletions and duplications within the coding region of the gene(s) tested. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by this methodology. Regions of high homology and repetitive regions may not be analyzed. This methodology will not detect low level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of our deletion/duplication assay may be reduced when DNA extracted by an outside laboratory is provided.

PDX1 sequencing and deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81403, 81404
Turn-around time:	4 weeks

Results:

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References:

1. Thomas IH, Saini NK, Adhikari A et al. Neonatal diabetes mellitus with pancreatic agenesis in an infant with homozygous IPF-1 Pro63fsX60 mutation. Pediatr Diabetes 2009: 10: 492-496.
2. Fajans SS, Bell GI, Paz VP et al. Obesity and hyperinsulinemia in a family with pancreatic agenesis and MODY caused by the IPF1 mutation Pro63fsX60. Transl Res 2010: 156: 7-14.

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