



GATA6 Analysis for Pancreatic Agenesis and Congenital Heart Defects

Clinical Features

Pancreatic Agenesis and Congenital Heart Defects [PACHD, OMIM#600001] is characterized by neonatal diabetes mellitus and congenital heart defects. Intrafamilial variability has been reported with regard to both severity of diabetes (ranging from neonatally lethal diabetes to adult-onset diabetes associated with agenesis of the pancreas) and the types of congenital cardiac defects in affected individuals (1). The most common congenital cardiac defects include atrial septal defects, ventral septal defects and tetralogy of fallot.

Molecular Genetics

Mutations in the *GATA6* [OMIM#601656] gene have been reported in patients with PACHD. Lango Allen *et al*, 2011 identified mutations in *GATA6* in 56% of subjects with pancreatic agenesis (2). *GATA6* is a member of a GATA family of zinc-finger transcriptional regulators, which bind to the common WGATAR motif in the regulatory regions of many genes.

Inheritance

Most cases appear to be *de novo*, but familial cases are reported. Recurrence risk for affected individuals with a *GATA6* mutation is 50%.

Test methods:

Comprehensive sequence coverage of the coding regions and splice junctions of the *GATA6* gene is performed. Targets of interests are captured and amplified using Agilent SureSelect target enrichment system. The constructed genomic DNA library is sequenced 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 novel and/or potentially 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 20bp. Deletion/duplication analysis of the *GATA6* gene is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

GATA6 sequencing

Sample specifications:	3 to 10 cc of blood in a purple top (EDTA) tube
Cost:	\$1000
CPT codes:	81405
Turn-around time:	4 weeks

GATA6 deletion/duplication analysis

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Cost:	\$1000
CPT codes:	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. Yorifuji T, Kawakita R, Hosokawa Y *et al*. Dominantly inherited diabetes mellitus caused by *GATA6* haploinsufficiency: variable intrafamilial presentation. *J Med Genet* 2012; 49: 642-643.
2. Lango Allen H, Flanagan SE, Shaw-Smith C *et al*. *GATA6* haploinsufficiency causes pancreatic agenesis in humans. *Nat Genet* 2012; 44: 20-22.

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