Clinical Features
Pancreatic Agenesis and Congenital Heart Defects [PACHD, OMIM#600001] is characterized by neonatal diabetes mellitus and congenital heart defects. Intrafamiliar variability has been reported with regard to both severity of diabetes (ranging from neonatal 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 WGAATAR 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 HaloPlex 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.

GATA6 sequencing
Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
Cost: $2200
CPT codes: 81405
Turn-around time: 4 weeks

GATA6 deletion/duplication analysis
Sample specifications: 3 to10 cc of blood in a purple top (EDTA) tube
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.

References: