THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

NEUROG3 Analysis for Neonatal Diabetes Mellitus with Severe Malabsorptive Diarrhea

Clinical Features and Molecular Genetics

Mutations in *NEUROG3* [OMIM#604882] are associated with congenital malabsorptive diarrhea, neonatal diabetes and impaired pancreatic exocrine function (1, 2). All reported cases present with chronic unremitting malabsorptive diarrhea in the first weeks of life. NEUROG3 is a transcription factor involved in the determination of neural precursor cells in the neuroectoderm, it is expressed in endocrine progenitor cells and is required for endocrine cell development in the pancreas and intestine(3).

Inheritance

NEUROG3 mutations follow an autosomal recessive inheritance pattern and are a rare cause of permanent neonatal diabetes mellitus. Parents of an affected child are most likely obligate carriers. Recurrence risk for carrier parents is 25%.

Test methods:

Comprehensive sequence coverage of the coding regions and splice junctions of the *NEUROG3* 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 *NEUROG3* 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.

NEUROG3 sequencing

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

NEUROG3 deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81403
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. Pinney SE, Oliver-Krasinski J, Ernst L et al. Neonatal diabetes and congenital malabsorptive diarrhea attributable to a novel mutation in the human neurogenin-3 gene coding sequence. J Clin Endocrinol Metab 2011: 96: 1960-1965.
2. Rubio-Cabezas O, Jensen JN, Hodgson MI et al. Permanent Neonatal Diabetes and Enteric Anendocrinosis Associated With Biallelic Mutations in NEUROG3. Diabetes 2011: 60: 1349-1353.
3. Wang J, Cortina G, Wu SV et al. Mutant neurogenin-3 in congenital malabsorptive diarrhea. N Engl J Med 2006: 355: 270-280.

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