CTNS sequence analysis and 57 kb deletion analysis

Disorder: Cystinosis is a rare autosomal recessive lysosomal storage disorder with an incidence of 1 per 100,000 to 200,000 live births. The gene associated with cystinosis (*CTNS*) is located at 17p13 and encodes the protein cystinosin which transports cystine out of the lysosome and into the cytoplasm. The most common mutation is the 57 kb deletion which includes exons 1-9 and part of exon 10 of *CTNS*. Homozygosity for the 57 kb deletion is very common, accounting for 46% to 75% of mutations in people of Northern European ancestry.

There are three clinical types of cystinosis:

Classic nephropathic cystinosis (95% of cases) (infantile/early onset):

- Growth retardation after six months
- Renal tubular Fanconi syndrome before age 1 and renal failure by age 10, if untreated
- Corneal cystine crystals observed through slit lamp examination
- Photophobia, hypothyroidism, diabetes mellitus, and hypogonadism in males

Intermediate cystinosis (juvenile/late onset)

- Same symptoms as those seen in classic cystinosis
- Symptoms with delayed onset and decreased severity
- Age of onset is later, generally between ages 15 and 25, with end-stage renal disease secondary to glomerular involvement

Non-nephropathic cystinosis

- Photophobia secondary to corneal cystine crystals
- No extraocular symptoms

Indications:

- Confirmation of diagnosis in patient with physical manifestation of cystinosis
- Presymptomatic diagnosis and/or carrier testing in a relative of a patient with proven *CTNS* mutation(s)
- Prenatal diagnosis of an at-risk fetus, after confirmation of biallelic mutations in the parents (by prior arrangement only)

Additional information and test requisitions are available at: www.cchmc.org/molecular-genetics

Shipping Instructions:

Please enclose **test requisition** with sample.
All information must be completed before sample can be processed.

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

Cincinnati Children's
Human Genetics

Molecular Genetics Laboratory
CLIA#: 36D0656333
Phone: (513) 636-4474
Fax: (513) 636-4373
Email: moleculargenetics@cchmc.org
www.cincinnatichildrens.org/molecular-genetics

Specimen:

Blood: 3mL whole blood in purple top (EDTA) tube.

Cytobrush (buccal sample): 6 cytobrushes sent at ambient temperature. Please call for free cytobrush collection kit.

Label each item with patient's name, birth date, and date of collection.

Testing Methodology:

Targeted analysis to identify the 57 kb deletion and/or Sanger sequencing following PCR amplification of the coding and exon/intron boundaries of the *CTNS* gene.

Test Sensitivity:

Clinical Sensitivity: *CTNS* is the only gene which is associated with cystinosis. Between 81-97% of patients with cystinosis have identifiable mutation(s) in *CTNS*. Patients with cystinosis in whom no mutation is identified by sequencing of the exons and exon/intron boundaries may have mutations deeper in the introns or within the promoter region of the *CTNS* gene. Large deletions (other than the common 57 kb deletion), insertions and other complex rearrangements are possible, but have not been reported.

Analytical Sensitivity: The sensitivity of DNA sequencing is greater than 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Mutations in regulatory regions or other untranslated regions are not detected by this test. Large deletions involving entire single exons or multiple exons, large insertions and other complex genetic events will not be identified using sequencing test methodology. The sensitivity of targeted 57kb deletion analysis is >99%. Rare primer site variants may lead to erroneous results.

Turn-Around Time:

Four weeks

CPT Codes:

CTNS full gene sequencing: 81479

CTNS 57 kb deletion analysis: 81479

Family specific mutation analysis: 81403

Please call 1-866-450-4198 for pricing, insurance preauthorization, or with any billing questions.

Results:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

References:

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