Congenital Hypothyroidism: *PAX8* Gene Deletion/Duplication

**Condition Description**

Congenital hypothyroidism occurs when the thyroid gland fails to develop or function properly. In 80-85% of cases, the thyroid gland is absent (agensis), ectopically located, and/or severely reduced in size (hypoplasia) [1]. In the remaining cases, a normal-sized or enlarged thyroid gland is present, but production of thyroid hormones is decreased or absent. If treatment begins in the first month after birth, infants usually develop normally. However, if thyroid hormone therapy is not initiated within the first two months of life, congenital hypothyroidism can cause severe neurological, mental, and motor damage (cretinism). In the United States and many other countries, all newborns are tested for congenital hypothyroidism.

Studies have shown that 2% of congenital hypothyroidism patients with thyroid dysgenesis have a positive familial history [2]. A segregation analysis led to the conclusion that thyroid developmental abnormalities are compatible with an autosomal dominant mode of inheritance with a low penetrance [3]. Mutations in many genes are known to cause congenital hypothyroidism. Multiple affected individuals have been shown to be heterozygous for mutations in the Paired Box Gene 8 (*PAX8* 2q12-q14), including individuals with positive family histories [4-8].

**References:**


**Genes**

*PAX8*

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of congenital hypothyroidism in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of congenital hypothyroidism who have tested negative for sequence analysis

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:

Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the *PAX8* gene is available and is required before deletion/duplication analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.