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**Lab Dept:**                    **Anatomic Pathology**

**Test Name:**                **CYP21A2 (CAH) EVALUATION SEQUENCING**

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***General Information***

**Lab Order Codes:**        CYP A

**Synonyms:**                Congenital Adrenal Hyperplasia Evaluation Sequencing; CYP21A2 Sequencing; 21-Hydroxylase Gene Sequencing

**CPT Codes:**                81405 – Molecular Pathology Level 6 (CYP21A2, full gene sequence)  
81402 – Molecular Pathology Level 3 (CYP21A2, common variants)

**Test Includes:**            Sanger sequencing and multiplex ligation-dependent probe amplification to evaluate the CYP21A2 gene for carrier screening and diagnosis of the 21-hydroxylase deficient congenital adrenal hyperplasia (CAH).

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***Logistics***

**Test Indications:**        Carrier screening and diagnosis of 21-hydroxylase deficient congenital adrenal hyperplasia (CAH) in individuals with a personal or family history of 21-hydroxylase deficiency, or as follow-up to positive CAH newborn screens/or measurement of basal and adrenocorticotrophic hormone-1-23 stimulated 17-hydroxyprogesterone, androstenedione, and other adrenal steroid levels.

May be used to identify CYP21A2 mutations in individuals with a suspected diagnosis of 21-hydroxylase deficient CAH when a common mutation panel is negative or only identifies 1 mutation.

In prenatal cases of ambiguous genitalia detected by ultrasound, particularly when the fetus is confirmed XX female by chromosome analysis.

This test code should also be used for known/familial variant analysis for CYP21A2. Due to the complexity of the CYP21A2 locus, site specific testing for known/familial variants is not offered for this gene.

**Lab Testing Section:**     Anatomic Pathology – Sendouts

**Referred to:**                Mayo Clinic Laboratories (MML: CYPZ)

**Phone Numbers:**         MIN Lab: 612-813-6280

STP Lab: 651-220-6550

**Test Availability:**         Daily, 24 hours

**Turnaround Time:** Performed weekly, results in 14-21 days.

**Special Instructions:** Mayo form T663 [CYP21A2 Gene Testing Patient Information Sheet](#) is strongly recommended. Provider to complete and lab to send with the specimen.

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### ***Specimen***

**Specimen Type:** Whole blood

**Container:** Lavender top (EDTA) tube

**Draw Volume:** 3 mL (Minimum: 1 mL) blood

**Processed Volume:** Same as Draw Volume

**Collection:** Routine venipuncture

**Special Processing:** Lab Staff: Do Not Centrifuge. Specimen should remain in the original collection container. Store and ship at room temperature. Forward promptly.

Specimen stable ambient (preferred) for 4 days, refrigerated for 14 days.

**Patient Preparation:** A previous bone marrow transplant from an allogenic donor will interfere with testing. Call Mayo line 1-800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

**Sample Rejection:** Mislabeled or unlabeled specimens; specimens other than EDTA whole blood

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### ***Interpretive***

**Reference Range:** An interpretive report will be provided.

**Limitations:**

Because of the complexity of the genetic structure of the CYP21A2 locus, and the possibility that a patient's congenital adrenal hyperplasia (CAH) may be due to other gene defects, genetic testing results should be correlated carefully with clinical and biochemical data.

This testing strategy is superior to approaches previously used, but may still miss some complex and large-scale genetic rearrangements or deletions, as well as genetic changes in far upstream or downstream gene-regulatory elements that impair CYP21A2 gene expression. This can lead to false-negative test results.

Rare polymorphisms in primer binding sites can lead to selective allelic drop-out, which can lead to false-negative or false-positive diagnosis.

Patients without genetic evidence for disease-causing CYP21A2 genetic changes may still suffer from CAH, but due to a different enzyme defect. Additional and expanded biochemical steroid profiling is, therefore, recommended if the clinical picture is strongly suggestive of CAH.

**Methodology:**

Polymerase Chain Reaction (PCR); Followed by DNA Sequence Analysis and Gene Dosage Analysis by Multiplex Ligation-Dependent Probe Amplification (MLPA)

**References:**

[Mayo Clinic Laboratories](#) June 2023

**Updates:**

1/13/2011: CPT update

4/5/2011: Test moved from Athena Diagnostics to Mayo Medical Laboratories.

2/5/2013: CPT update

4/10/2017: CPT and test update

6/20/2023: Added notice regarding temporary test delays at Mayo; added specimen stability; added patient preparation for bone marrow transplant patients.

3/7/2024: Removed notice about testing delay. Normal turnaround times have resumed.