MAYO CLINIC LABORATORIES

1-800-533-1710

CYPZ

21-Hydroxylase Gene (CYP21A2), Full Gene Analysis

Patient ID	Patient Name		Birth Date	Gender	Age
SA00085580	TESTINGRNV, CYPZNORM		1966-06-10	F	50
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00085580	SA00085580	CLIENT, CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		08 Feb 2017 13:00			

CYP21A2 Gene, Full Gene Analysis

Result Summary

MCR

NEGATIVE

Result

MCR

MLPA DETECTED THE FOLLOWING:

Two copies of the CYP21A2 gene
Two copies of the inactive CYP21A1P pseudogene

No reportable sequence variants were identified by sequence analysis of the CYP21A2 gene.

Interpretation

1 MCR

This result decreases the likelihood of, but does not rule out, carrier or affected status for 21-hydroxylase deficient congenital adrenal hyperplasia (CAH). Some individuals who are carriers of, or affected with, 21-hydroxylase deficient congenital adrenal hyperplasia may have a pathogenic CYP21A2 variant(s) that are not detectable by the methods utilized. Additionally, the clinical phenotype that is observed in this individual and/or family may be due to a pathogenic variant(s) in another gene(s).

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing. If testing was performed due to a family history of 21-hydroxylase deficient congenital adrenal hyperplasia, genetic testing of an affected family member is necessary to determine whether this test is of predictive value for this family. Identification of the pathogenic variant in this family would allow for more accurate risk assessment of at risk individuals.

Unless reported or predicted to cause disease, alterations found deep in the intron or alterations that do not result in an amino acid substitution are not reported. These and common benign variants identified for this patient are available upon request.

In most cases, one copy of the CYP21A2 gene and one copy of its highly homologous, inactive pseudogene CYP21A1P are separated by approximately 30 kb on chromosome 6. When two copies of the CYP21A2 gene are present, they are typically in trans (on opposite alleles). However, the CYP21A2 locus is prone to large rearrangements due to the proximity of CYP21A2 and CYP21A1P. Therefore, unless otherwise stated in the interpretation, the technology used here is unable to confirm the phase (cis/trans arrangement) of any identified copies of CYP21A2, CYP21A1P, or hybrid alleles. Family studies of blood relatives might assist in determination of phase.

A genetic consultation may be of benefit.

ADDITIONAL INFORMATION

A combined testing approach involving PCR amplification, bi-directional sequence analysis, and multiplex ligation-dependent probe amplification (MLPA) is used to identify sequence variants and copy number variation within the CYP21A2 gene (GenBank accession number NM_000500; build GRCh37 (hg19)).

Four sets of PCR primer pairs amplify the CYP21A2 gene, the inactive CYP21A1P pseudogene, and the CYP21A2/CYP21A1P and CYP21A1P/CYP21A2 hybrids to determine the presence or absence of amplification product.

Bi-directional full gene sequence analysis, including a portion of the promoter and 3-prime untranslated regions, is then performed on the CYP21A2 gene and the CYP21A2/CYP21A1P hybrid (if present) to test for the presence of sequence variants. Because the CYP21A1P/CYP21A2 hybrid and the CYP21A1P pseudogene are expected to be inactive, sequencing is not performed unless required for interpretation.

MLPA is performed to determine the copy number of the 5-prime and 3-prime regions of the CYP21A2 gene and the CYP21A1P pseudogene. Quantification and comparison of results is used to determine the copy number of the CYP21A2 gene, the CYP21A1P pseudogene, and the CYP21A2/CYP21A1P and CYP21A1P/CYP21A2 hybrids. Correlation of results from PCR, bi-directional sequencing, and MLPA is used to determine the CYP21A2 genotype. An online research opportunity called GenomeConnect (genomeconnect.org), a project of ClinGen, is available for the recipient of this genetic test. This patient registry collects de-identified genetic and health information to advance the knowledge of genetic variants. Mayo Clinic is a collaborator of ClinGen. This may not be applicable for all tests.

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	William G. Morice M.D. Ph.D	24D0404292

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Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Bone Marrow transplants from allogenic donors will interfere with testing. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Multiple in-silico evaluation tools may have been used to assist in the interpretation of these results. Of note, the sensitivity and specificity of these tools for the determination of pathogenicity is currently unvalidated.

Specimen MCR

WB Whole Blood

Released By MCR

Alicia Algeciras-Schimnich,Ph.D.

Received: 09 Feb 2017 13:43 **Reported:** 14 Feb 2017 17:01

Laboratory Notes

1 This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

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