**ARUP LABORATORIES | aruplab.com**
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: 801-583-2787, toll free: 800-522-2787
Jonathan R. Genzen, MD, PhD, Chief Medical Officer

**PATIENT REPORT**

Patient Age/Sex: Male

**Specimen Collected: 05-Aug-22 08:46**

**Hereditary Polycythemia Panel by NGS** | **Received: 05-Aug-22 08:46** | **Report/Verified: 05-Aug-22 08:59**

| Procedure | Result | Units | Reference Interval |
|---|---|---|---|
| ECYT Interp | Negative [i1] | | |
| ECYT Specimen | Whole Blood | | |

## Test Information

i1: ECYT Interp

BACKGROUND INFORMATION: Hereditary Erythrocytosis Panel, Sequencing

CHARACTERISTICS: Hereditary erythrocytosis, also known as familial erythrocytosis or congenital polycythemia, is a group of disorders in which inherited/germline pathogenic variants cause increased red blood cell (RBC) production, leading to elevated hemoglobin and hematocrit levels. Symptoms may include headaches, dizziness, dyspnea, and epistaxis. Overabundance of RBC may lead to hemorrhagic or thrombotic events, including myocardial infarction and deep vein thrombosis, although many individuals with erythrocytosis experience mild symptoms and may even be asymptomatic. Hereditary erythrocytosis can be categorized as primary, caused by pathogenic variants leading to intrinsic defects in hematopoietic stem cells that increase RBC production, or secondary caused by pathogenic variants that drive RBC production by increasing erythropoietin (EPO). Hereditary erythrocytosis is suspected in individuals for whom acquired erythrocytosis (either primary or secondary) has been excluded, and in those with early age of onset or a family history of erythrocytosis.

EPIDEMIOLOGY: Hereditary erythrocytosis is rare but the exact prevalence is unknown. Up to 70 percent of cases have no identified cause and are classified as idiopathic erythrocytosis.

CAUSE: Pathogenic germline variants in genes associated with erythrocytosis

INHERITANCE: Mostly autosomal dominant with some autosomal recessive disorders

GENES TESTED: BPGM, EGLN1 (PHD2), EPAS1 (HIF2), EPOR, HBB, HIF1A, JAK2, SH2B3, VHL*
*One or more exons are not covered by sequencing for the indicated gene; see limitations section below.

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and to confirm reported variants that do not meet acceptable quality metrics. Human genome build 19 (Hg 19) was used for data analysis.

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i1: ECYT Interp

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions (indels) from 1-10 base pairs in size. Indels greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. Specificity is greater than 99.9 percent for all variant classes.

LIMITATIONS: A negative result does not exclude a diagnosis of erythrocytosis. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Regulatory region variants, deep intronic variants, and large deletions/duplications will not be identified. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations caused by the presence of pseudogenes, repetitive, or homologous regions. This test is not intended to detect low-level mosaic variants, gene conversion events, complex inversions, translocations, mitochondrial DNA (mtDNA) mutations, or repeat expansions. This assay is also not intended to detect somatic variants associated with hematologic malignancy, though such variants may be detected incidentally. Though this test is designed to identify germline variants associated with erythrocytosis, it cannot definitively determine the germline or somatic origin of detected variants when the patient has acquired erythrocytosis or hematologic malignancy and the assay is performed on blood or other tissue that may be contaminated by clonal or malignant cells. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

SNVs and indels will not be called in the following regions due to technical limitations of the assay: VHL (NM_001354723) exon 2

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. This test was performed in a CLIA-certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.