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CAP ACCREDITED

LABORATORY REPORT

| PATIENT | SPECIMEN | PHYSICIAN |
|---|---|---|
| Name:<br>Address:<br><br>Phone Number:<br><br>Accession #: | Specimen Type:<br><br>Received Date: 05/16/24<br><br>Reported Date: 05/19/24 | Name:<br><br>Address:<br><br>Phone: |

# VEXAS Test Report

## Summary of Results: POSITIVE (*UBA1* Mutation Detected)

### *INTERPRETATION:*

This patient tested positive for one of the eight (8) known hotspot mutations that have been identified in patients with VEXAS (Vacuoles. E1. X-Linked, Autoinflammatory, Somatic Syndrome) to date (see table below). It confirms the clinical diagnosis of VEXAS syndrome. VEXAS-associated pathogenic variants are acquired and occur in the bone marrow progenitor cells rather than in the germline cells. This means that they are unlikely to be shared with parents, siblings, children, or other family members.

| Gene | Location | Amino acid change | Nucleotide change | Detected (Y/N) |
|---|---|---|---|---|
| *UBA1* | Intron 2 | n/a | c.118-2A>C | N |
| *UBA1* | Intron 2 | n/a | c.118-1G>C | N |
| *UBA1* | Intron 2 | n/a | c.118-9_118-2del | N |
| *UBA1* | Exon 3 | p.M41T | c.122T>C | Y |
| *UBA1* | Exon 3 | p.M41V | c.121A>G | N |
| *UBA1* | Exon 3 | p.M41L | c.121A>C | N |
| *UBA1* | Exon 3 | p.S56F | c.167C>T | N |
| *UBA1* | Exon 16 | p.S621C | c.1861A>T | N |

## *Assay Description and Performance*

The QClamp® Plex VEXAS Syndrome Test (in short, VEXAS Test) is a qualitative genetic test for the simultaneous detection of eight (8) syndrome-associated somatic mutations of UBA1 genes associated with VEXAS Syndrome. The assay uses genomic DNA extracted from peripheral blood (or bone marrow), amplified using target-specific pooled primer set to enrich mutant targets, followed by using ligation probes to amplify and label mutant targets with biotin and streptavidin phycoerythrin conjugate (SAPE)-conjugated magnetic beads, and analyze the UBA1 mutations with the Luminex system.

The detection limit for this assay for all eight mutations ranges from 0.10% to 5.0% of variant allele frequency (VAF): for M41T at 0.10%, M41V at 0.10%, M41L at 0.25%, c.118-2A>C at 1.0%, c.118-1G>C at 5.0%, c.118- 9_118-2del at 1.0%, S56F at 0.25%, and S621C at 1.0%, respectively. The assay will not detect other potential genetic alterations outside of the specified targets listed in the table above. Because of the superior sensitivity, the need to obtain bone marrow sample is obviated, and the mutations can be detected in the patient's peripheral blood samples.

## *Indication for Use*

The QClamp® Plex VEXAS Syndrome Test is a molecular Laboratory Developed Test (LDT) for the quantitative detection of eight syndrome-associated somatic mutations of UBA1 genes associated with VEXAS Syndrome from genomic DNA extracted from peripheral blood or bone marrow. It is to confirm the clinical diagnosis of VEXAS Syndrome (Vacuoles. E1. X-Linked, Autoinflammatory, Somatic Syndrome). This test is intended for patients with clinical symptoms and other pertinent laboratory findings raising concern for VEXAS syndrome, which may include, but are not limited to, systemic or localized (e.g., ear, orbital, skin) tissue inflammation presenting as rheumatologic disease, abnormal (usually low) whole blood counts, macrocytic anemia, characteristic microscopic changes in the bone marrow, as well as others.

## *Disclaimer*

The QClamp® Plex VEXAS Syndrome Test is performed at the DiaCarta Clinical Laboratory as a Laboratory Developed Test (LDT). It was developed by DiaCarta with performance characteristics determined by DiaCarta, based on clinical studies on radiation toxicity assessment on prostate cancer patients. The test is not cleared or approved by the U.S. Food and Drug Administration (FDA). This test has been validated at the DiaCarta Clinical Laboratory pursuant to CLIA regulations and can be used for clinical purposes. The test results may be used along with other therapies and cancer types, but the result interpretation has not been validated and should be used with caution by medical professionals. This test has not been investigated or validated for use in inhaled radiation. DiaCarta is not responsible for the clinical decisions made based on this test. The DiaCarta Clinical laboratory is regulated under CLIA regulations and is qualified to perform high-complexity testing.

## *References:*

1. Hagiya A, et al. How Do I Diagnose and Manage VEXAS Syndrome. Am J Clin Pathol. 2024 Mar 21. PMID: 38511841.
2. Ma YQ, et al. A novel XNA-based Luminex assay to detect UBA1 somatic mutations associated with VEXAS syndrome. Practical Laboratory Medicine 39 (2024) e00380.
3. Beck DB, et al. Somatic mutations in UBA1 and severe adult-onset autoinflammatory disease, N. Engl. J. Med. 383 (27) (2020) 2628–2638.
4. Beck DB, et al. Estimated Prevalence and Clinical Manifestations of UBA1 Variants Associated with VEXAS Syndrome in a Clinical Population. JAMA. 2023;329(4):318-324.