

Date: July 10, 2025

To: All BC Cancer Staff and/ or rheumatologists, hematopathologists, hematologists

From: Stephen Yip, M.D., Ph.D., FRCPC  
Medical Director – Cancer Genetics & Genomics Laboratory  
Medical Director – Centre for Clinical Genomics

**RE: Launch of *UBA1* mutation screening at CGL**

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This letter is to inform you that effective **July 21<sup>st</sup>, 2025**, the Cancer Genetics and Genomics Laboratory (CGL) at BC Cancer will be offering NGS based *UBA1* mutation testing for patients with suspected VEXAS\* syndrome. Identified variants will be reported out based on their clinical impact using AMP/ASCO/CAP guidelines.<sup>1</sup>

\*VEXAS: Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic

### What is detected by this test?

This test enables the accurate assessment of genomic variants (SNVs and small indels only) over the entire coding region of *UBA1*.

### Who qualifies for testing?

Individuals who are suspected to have VEXAS syndrome based on a combination of clinical and morphologic criteria, as determined by a hematologist, rheumatologist, and/or hematopathologist.

### How is the test ordered?

VEXAS can be ordered using the CGL Myeloid Requisition ([link](#)).

Testing is restricted to rheumatologists, hematopathologists, and hematologists.

### What sample is required?

Bone marrow aspirate (DNA): 1 x 0.5ml in EDTA tube

**OR**

Peripheral blood (DNA): 1 x 6ml EDTA tube

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- For CST Cerner: Order 'LAB-Miscellaneous Test (Blood)' → indicate "VEXAS-EDTA" in the 'Name of the Lab test' field
- For non-CST Cerner: Patients can bring printed requisition to any phlebotomy laboratory for blood sample collection.

**Note:** If a sample has already been submitted to CGL for Myeloid Panel testing, VEXAS testing can be initiated on the existing sample, and no additional sample collection will be required. The requestor will complete requisition by entering the date of the previous collection in the 'Collection Date' field or the associated SHIRE number in the 'Referring Lab/ Hospital Sample ID' field.

Peripheral blood is generally sensitive for identifying *UBA1* mutations as these are found at high variant allele frequency in the peripheral blood. A bone marrow aspirate is not required for the initiation of testing. This test offering is separate from the myeloid somatic NGS panel, and does not include other potentially relevant myeloid genes (e.g., *DNMT3A*, *TET2*, etc.) – if myeloid NGS testing is required, this must be ordered separately.

## Where and how does the sample get sent?

Further information: <https://cancergeneticslab.ca/guidelines/specimens/#Shipping>

Cancer Genetics and Genomics Laboratory

BC Cancer - Vancouver

Room #3307 – 600 West 10th Avenue

Vancouver, BC

V5Z 4E6

Ship at room temperature.

Maximum transit time from collection: 7 days

## How will the test be reported?

Variants identified by NGS at a variant allele frequency (VAF) of 5% or higher will be interpreted and categorized based on their clinical impact using AMP/ASCO/CAP guidelines (PMID: 27993330)<sup>1</sup> as follows:

Tier I: variants with strong clinical significance (level A and B evidence)

Tier II: variants with potential clinical significance (level C and D evidence)

- None anticipated
- Tier IIIA: variant of functional but with uncertain clinical significance
- None anticipated
- Tier IIIB: variants with uncertain function
- Tier IV: variants deemed to be (likely) benign
- Not typically reported

### What is the expected turn-around-time (TAT) for results?

The anticipated TAT testing is 21 days from receipt of the sample in CGL.

### How can I access the clinical report results for my patient?

The clinical report will be:

- Generated using the CGL SHIRE platform which is used for all CGL reporting
- Uploaded electronically to CAIS, CST Cerner, and CareConnect
  - For CareConnect information on how to view the report or to request access, [click here](#)
- Mailed as a paper copy via Canada Post unless previously opted out
  - To discontinue receipt of the mailed paper copy, [complete this form](#)

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### Questions

Email: [cancergeneticslab@bccancer.bc.ca](mailto:cancergeneticslab@bccancer.bc.ca)

Website: [cancergeneticslab.ca](http://cancergeneticslab.ca)

### References

1. Li, MM. *et al.* Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. *J Mol Diag.* (2017) **1**, 4-23. (PMID: 27993330)
2. Beck, DB. *et al.* Somatic Mutations in *UBA1* and Severe Adult-Onset Autoinflammatory Disease. *NEJM* (2020) **383**, 2628-2638. (PMID: 33108101)
3. Stubbins, RJ. *et al.* Innovations in Genomics for Undiagnosed Diseases: Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic (VEXAS) Syndrome. *CMAJ* (2022) **194**, E524-E527. (PMID: 35410861)

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4. Beck, DB. *et al.* Estimated Prevalence and Clinical Manifestations of UBA1 Variants Associated With VEXAS Syndrome in a Clinical Population. *JAMA* (2023) **329**,318-324 (PMID: 36692560)
5. Koster, MJ. *et al.* VEXAS syndrome: Clinical, hematologic features and a practical approach to diagnosis and management. *Am J Hematol* (2023) **99**, 284-299. (PMID: 37950858)
6. Baumbach-Reardon, L. *et al.* Spinal Muscular Atrophy, X-Linked Infantile. (2024) GeneReviews. <https://www.ncbi.nlm.nih.gov/books/NBK2594/>