

DATE:	12 December 2022
TO:	All Zones
FROM:	APL Genetics and Genomics, Molecular Genetics (North and South)
RE:	Tumour Testing Results Required for Germline Lynch Syndrome Genetic Testing

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Key Message

- To be eligible for germline genetic testing for Lynch syndrome patients must have tumour testing results suggestive of Lynch syndrome OR meet Amsterdam criteria. Immunohistochemistry (IHC) results determine the appropriate testing algorithm and must be provided on the requisition.

How this will impact you

- For patients meeting Amsterdam criteria, include tumor testing results if available.
- For patients who do not meet Amsterdam criteria and have a personal history of colon cancer or endometrial cancer, IHC results are required.
- When MLH1 or MLH1/PMS2 are absent:
 - *MLH1* promoter hypermethylation results are required for colon and endometrial cancers
 - *BRAF* results are required for colon cancers if MLH1 promoter hypermethylation results are not available
 - When the *BRAF* V600E mutation or *MLH1* promoter hypermethylation is detected in a tumour with absence of MLH1 and/or PMS2, the cancer is likely sporadic. Germline genetic testing is generally not indicated. If there is a young age of onset or significant family history, consider referral to Genetics.
- For patients who are <45 years of age with colon or endometrial cancer and normal IHC, consider Microsatellite Instability (MSI) testing. If high microsatellite (MSI-H) instability is detected, the patient is eligible for germline genetic testing. MSI results must be provided on the requisition. In patients with low microsatellite instability (MSI-L) or microsatellite stable (MSS) tumours, germline genetic testing is not indicated.
- IHC results impact reflex testing and are required to ensure that all indicated testing is completed. If sequencing does not detect a likely pathogenic or pathogenic variant:
 - *MSH2* MLPA will be performed when IHC reveals absence of MSH2 or MSH6
 - *PMS2* MLPA will be performed when IHC reveals absence of PMS2
- Samples with incomplete clinical information including tumour test results will be cancelled and discarded.

Action Required

- Include all required clinical information and tumour test results on the requisition as outlined above
- If above information is not included on the requisition, testing will be cancelled, and sample discarded. If tumour testing results are not consistent with Lynch syndrome, testing will be cancelled, and sample discarded.

Effective

December 12, 2022



Questions/Concerns

- Molecular Genetics Laboratory Genetic Counsellors
 - *North* 780-407-1015
 - *South* 403-955-3097

Approved by

- Dr. Dennis Bulman, Medical/Scientific Director, Provincial Genetics and Genomics Program, APL
- Dr. Carolyn O'Hara, Chief Medical Laboratory Officer (Interim), APL