ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Lynch Syndrome Panel: Information for Ordering Providers

In general, the lifetime risk to develop colon cancer in Canada is 1 in 16 (6.1%) for men and 1 in 19 (5.3%) for women[1]. Most colon cancers occur sporadically. Approximately 5-10% of colon cancers are related to a hereditary cancer syndrome. Lynch syndrome is a hereditary cancer syndrome which is associated with an increased risk for multiple cancers including colon, ovarian, and uterine. Approximately 2-4%[2] of colon cancers and 2.5% of uterine cancers[2] are due to Lynch syndrome.

Alberta has a universal Lynch syndrome screening program for all patients with a new diagnosis of colorectal cancer, or endometrioid/undifferentiated endometrial or ovarian carcinomas using tumour immunohistochemistry (IHC).

Lynch syndrome can also be diagnosed using the Amsterdam criteria. All the following must be met:

- three or more relatives with a histologically verified Lynch Syndrome-associated cancer, one of whom is a first-degree relative of the other two
- affecting at least two successive generations
- one or more cases diagnosed before the age of 50

Indications for Testing

Testing should be considered in affected individuals who

- have abnormal tumour IHC suggestive of Lynch syndrome OR
- meet Amsterdam criteria

Ordering privileges

Please refer to the APL Test Directory (http://ahsweb.ca/lab/apl-td-lab-test-directory) for specific ordering restrictions.

Lynch Syndrome NGS Panel

This panel includes five genes known to cause Lynch Syndrome: *MLH1*, *MSH2, MSH6*, *PMS2* and *EPCAM*. Analysis of the *EPCAM* gene includes copy number analysis only.

Reflex testing for *PMS2* (exons 11-15) will only be performed if no pathogenic variant is detected and *PMS2* was absent by IHC.

Reflex testing by *MSH2* Multiplex Ligation-dependent Probe Amplification (MLPA) will only be performed if no pathogenic variant is detected and MSH2 or MSH6 was absent by IHC.

IHC results *must* be noted on the requisition form to ensure appropriate reflex testing is performed.

Associated Disorders[3]

Hereditary cancer predispositions are typically inherited in an autosomal dominant fashion. Some of the genes on these panels are associated with other rare disorders including:

> **Constitutional mismatch repair deficiency syndrome** is a rare autosomal recessive condition that occurs in individuals who have two pathogenic variants in one of the following genes: *EPCAM, MLH1, MSH2, MSH6 or PMS2.* Affected individuals often have onset of colon/intestinal cancer before the age of 20 years and may have a cutaneous phenotype similar to that seen in neurofibromatosis type I.

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When can I expect results?
Results may take up to 4 months.

How are results reported?
Results are sent to the ordering provider and available in Netcare and Connect Care.

Contact Information
Genetic Counsellors, Genetics & Genomics
Edmonton: 780-407-1015
Calgary: 403-955-3097

Requisition forms, contact information and other resources can be found at:
http://ahsweb.ca/lab/if-lab-genetics-and-genomics

References

1. Canadian Cancer Statistics Advisory Committee in collaboration with the Canadian Cancer Society, Statistics Canada and the Public Health Agency of Canada. Canadian Cancer Statistics 2021. Toronto, ON: Canadian Cancer Society; 2021. Available at: cancer.ca/Canadian-Cancer-Statistics-2021-EN (accessed [2022 September])
2. Bhattacharya P, McHugh TW. Lynch Syndrome. 2022 Jul 18. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 28613748.
3. Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1211/ (accessed [2022 September])