



In general, women have a 1 in 8 (12.5%) risk of breast cancer and a 1 in 79 (1.3%) risk of ovarian cancer during their lifetime.¹ Approximately 5-10% of breast cancers and up to 25% of ovarian cancers are associated with a pathogenic variant in a single cancer predisposition gene.^{2,3} Features suggestive of a hereditary cancer predisposition include:

- younger age at diagnosis
- multiple primary cancers in a single individual
- several relatives affected with related cancers spanning multiple generations

Individuals who carry a pathogenic variant in a hereditary cancer gene have an increased risk of certain cancers compared to the general population. Cancer risks depend on the gene(s) in which the variant(s) is identified. These individuals are eligible for increased cancer screening and/or risk reducing surgeries and therapeutic interventions. In addition, results may influence treatment plans for individuals with cancer.

If a pathogenic variant is identified in one of these genes, the patient and/or their family members may be at increased risk for specific cancers or other conditions. Genetic counselling is recommended for these families.

Indications for Testing

Patients with a personal and/or family history suggestive of a predisposition to breast and/or ovarian cancer may be eligible for testing.

Ordering Privileges

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

Breast and Ovarian Cancer NGS Panels

Genes	Breast Ovarian Cancer Panel, Core	Breast Ovarian Cancer Panel, Extended	Ovarian Cancer Panel
High-risk			
<i>EPCAM</i>			✓
<i>MLH1</i>			✓
<i>MSH2</i>			✓
<i>MSH6</i>			✓
<i>PMS2</i>			✓
<i>BRCA1</i>	✓	✓	✓
<i>BRCA2</i>	✓	✓	✓
<i>CDH1</i>	✓	✓	✓
<i>PTEN</i>	✓	✓	✓
<i>STK11</i>	✓	✓	✓
<i>TP53</i>	✓	✓	✓
Moderate-risk			
<i>ATM</i>		✓	✓
<i>BRIP1</i>		✓	✓
<i>CHEK2</i>		✓	✓
<i>NBN</i>		✓	✓
<i>PALB2</i>		✓	✓
<i>RAD51C</i>		✓	✓
<i>RAD51D</i>		✓	✓

High-risk genes:

- Associated with significantly increased cancer risks
- Clinical practice/management guidelines are available

Moderate-risk genes:

- Associated with moderately increased cancer risks
- Limited practice/management guidelines are available

Associated Disorders⁴

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:

Ataxia telangiectasia is an autosomal recessive disorder caused by pathogenic variants in the *ATM* gene. It is characterized by progressive cerebellar ataxia, telangiectasias, immunodeficiency and an increased risk for malignancy.

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.

Fanconi anemia (FA) can be inherited in an autosomal recessive, autosomal dominant or X-linked fashion. It is characterized by variable physical anomalies including short stature and skeletal limb malformations, bone marrow failure and an increased risk for malignancy. FA-associated genes on these panels include: *BRCA2*, *BRIP1*, *PALB2*, *RAD51C*.

PTEN hamartoma tumor syndrome (PHTS) is characterized by hamartomatous tumors and a germline *PTEN* pathogenic variant. PHTS includes Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, *PTEN*-related Proteus syndrome and Proteus-like syndrome.

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 July]).
2. American Cancer Society. Breast Cancer Risk Factors You Cannot Change. <https://www.cancer.org/cancer/breast-cancer/risk-and-prevention/breast-cancer-risk-factors-you-cannot-change.html#:~:text=About%20%25%20to%2010%25%20of,the%20BRCA1%20or%20BRCA2%20gene.> (accessed [2022 July])
3. American Cancer Society. Ovarian Cancer Risk Factors. <https://www.cancer.org/cancer/ovarian-cancer/causes-risks-prevention/risk-factors.html> (accessed [2022 July])
4. 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/NBK1116/> (accessed [2022 July])