



Approximately 15% of individuals in Canada will develop skin cancer in their lifetime, most often, basal cell carcinoma or squamous cell carcinoma.¹ Invasive melanoma occurs in an estimated 5% of individuals with skin cancer.¹ In some cases, skin cancers are associated with a pathogenic variant in a single cancer predisposition gene. 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.

Indications for Testing

Patients presenting with features of one of the syndromes listed below are 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.

Skin Cancer NGS panel

| Gene(s) | Associated cancers and/or clinical features ² | Associated Hereditary Syndrome ³ |
|---------------------|---|---|
| <i>CDK4, CDKN2A</i> | Multiple melanocytic nevi (often greater than 50 nevi), multiple primary melanomas, increased risk for pancreatic cancer. | Familial Atypical Multiple Mole Melanoma Syndrome |
| <i>CYLD</i> | Multiple skin tumors, typically located in the head and neck region, including cylindromas, trichoepitheliomas and spiradenomas. These tumors are typically benign but occasionally may become malignant. | Brooke-Spiegler syndrome |
| <i>PTCH1, SUFU</i> | Multiple jaw keratocysts and/or basal cell carcinoma, characteristic facial appearance (~60%), skeletal anomalies, medulloblastoma. | Nevoid Basal Cell Carcinoma syndrome |
| <i>BAP1</i> | A newly described gene that has been identified in families with renal cancer, uveal melanoma, cutaneous melanoma. While lifetime cancer risks are increased, they are not yet well defined. | <i>BAP1</i> tumour predisposition syndrome |

Associated Disorders²

The disorders on this panel either occur as a *de novo* condition or are inherited in an autosomal dominant fashion. Pathogenic variants in *PTCH1* have also been described in some individuals with holoprosencephaly and microcephaly.

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

Genetics Counsellors, Genetics & Genomics

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. Government of Canada. Skin cancer. <https://www.canada.ca/en/public-health/services/sun-safety/skin-cancer.html> (accessed [2022 September])
2. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018 [cited 2017 Dec]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK11116/>
3. Online Mendelian Inheritance in Man, OMIM® . McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), Available from: <https://omim.org/> (accessed [2022 September])