ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Fanconi Anemia and DNA Repair Disorders: Information for Ordering Providers

A number of hereditary diseases are characterized by defects in DNA repair including:

Fanconi Anemia (FA) [1] is characterized by physical abnormalities (stature and skeletal limb malformations), bone marrow failure and an increased risk for malignancy. A diagnosis of FA can be established in a patient with increased chromosomal breakage OR a pathogenic variant(s) in a gene known to cause FA. FA is associated with a number of genes, the majority of which are inherited in an autosomal recessive fashion. FA can also be inherited in an autosomal dominant or X-linked manner.

Ataxia Telangiectasia (A-T)[1] is characterized by progressive cerebellar ataxia, telangiectasias, immunodeficiency and an increased risk for malignancy. A-T is inherited in an autosomal recessive manner and is caused by pathogenic variants in *ATM*.

Bloom Syndrome[1] is characterized by severe prenatal and postnatal growth retardation, sun-sensitive facial erythema and predisposition to multiple cancers. Bloom syndrome is inherited in an autosomal recessive manner and is caused by pathogenic variants in *BLM*.

Nijmegen Breakage Syndrome (NBS)[1] is characterized by microcephaly, short stature, immunodeficiency and predisposition to cancer. NBS is inherited in an autosomal recessive manner and is caused by pathogenic variants in *NBN*.

***RECQL4*-related Disorders**[1] include Rothmund-Thomson syndrome, Baller-Gerold syndrome and RAPADILINO syndrome. These syndromes all include radial ray defects, skeletal abnormalities, slow growth/short stature and an increased risk for malignancy. They are inherited in an autosomal recessive manner and are caused by pathogenic variants in *RECQL4*.

Indications for Testing

Patients presenting with a personal and/or family history suggestive of one of the above syndromes are eligible for testing.

Molecular testing may be considered in situations where cytogenetic testing for FA or chromosomal breakage is not feasible or where cytogenetic testing is positive and identification of the specific variant is valuable.

Limitations

In individuals with a hematological malignancy, genetic testing may reveal a variant that is acquired rather than inherited. Confirmatory testing on another tissue (buccal, skin or urine) or a family member may be required.

Ordering Privileges

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

The genes included on the Fanconi Anemia NGS panel are:

BRCA2 (FANCD1)	*BRIP1 (FANCJ)*	*FANCA*	*FANCB*	*FANCC*	*FANCD2*	*FANCE*
FANCF	*FANCG*	*FANCI*	*FANCL*	*FANCM*	*PALB2 (FANCN)*	*RAD51C (FANCO)*
SLX4 (FANCP)	*ERCC4 (FANCQ)*	*ATM*	*BLM*	*NBN*	*RECQL4*	

Associated Disorders[2]

Hereditary Cancer: Some of the genes on this panel are associated with hereditary cancer. *BRCA2*, *BRIP1*, *ATM PALB2*, and *RAD51C* are associated with an increased risk of breast and/or ovarian cancer and/or pancreatic cancer. These hereditary cancer predispositions are inherited in an autosomal dominant manner.

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. 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. Genetic counselling is recommended for these families.

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.

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

Contact Information

Genetic Counsellors, Genetics & Genomics
Edmonton: 780-407-1015

References

1. 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 August])
2. NCCN Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: breast, ovarian and pancreatic. Version 2.2022 – March 9, 2022