ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Xeroderma Pigmentosum Panel: Information for Ordering Providers

Xeroderma pigmentosum is characterized by dermatological sun sensitivity, sunlight-induced ocular issues and an increased risk of sunlight-induced cancers such as basal cell carcinoma, squamous cell carcinoma, and melanoma. Approximately 25% of affected individuals also have neurologic abnormalities such as acquired microcephaly, progressive cognitive impairment, absent or diminished deep tendon reflexes, and progressive sensorineural hearing loss.[1]

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

Individuals with clinical findings of xeroderma pigmentosum are eligible for this panel test.

Ordering privileges

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

Xeroderma Pigmentosum NGS Panel

This panel includes seven genes known to cause xeroderma pigmentosum:

DDB2	*ERCC2*	*ERCC3*	*ERCC4*	*ERCC5*	*XPA*	*XPC*

Associated Disorders[1,2]

Xeroderma pigmentosum (XP) is inherited in an autosomal recessive fashion. There are a number of rare conditions with overlapping phenotypes that also exhibit cutaneous photosensitivity. Those that may be detected by this panel are as follows:

Cerebrooculofacioskeletal syndrome (COFS, also known as Pena-Shokeir syndrome type II), is an autosomal recessive condition due to pathogenic variants in *ERCC2*, *ERCC5* and *ERCC6*. This is a progressive neurologic disorder with microcephaly, growth failure, joint contractures and ocular findings. Of note, *ERCC6* is not included on this panel

Cockayne syndrome (CS), is an autosomal recessive condition due to pathogenic variants in *ERCC6* and *ERCC8* and is characterized by onset of growth and developmental anomalies in the first two years of life, along with progressive impairment of vision, hearing and nervous system function. Rarely, affected individuals have been found to have pathogenic variants detected in *ERCC4*. Of note, *ERCC6* is not included on this panel.

Fanconi anemia (FA) is characterized by variable physical anomalies including short stature and skeletal limb malformations, bone marrow failure, and an increased risk for malignancy. It can be inherited in an autosomal recessive, autosomal dominant, or X-linked fashion. *ERCC4* pathogenic variants can be associated with FA. *Please see our Fanconi anemia NGS panel information sheet to learn more about additional testing options for FA.*

Trichothiodystrophy (TTD) is an autosomal recessive condition caused by pathogenic variants in *ERCC3* and *ERCC2,* as well as other genes. Affected individuals have a variable phenotype which may include photosensitivity, ichthyosis, brittle hair, intellectual disability, short stature and distinctive facial features.

XFE progeroid syndrome has been described in one patient with homozygous pathogenic variants in *ERCC4*. It is not clear if this is a distinct condition or is part of a spectrum of XP, FA, or CS.

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
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. 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/NBK1116/

2. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [cited 2022 Sept]. Available from: https://medlineplus.gov/