ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Pediatric Cancer Panel: Information for Ordering Providers

The majority of pediatric cancers are sporadic; however, about 5% are thought to be due to a hereditary predisposition.[1] The disorders represented on this panel are typically *de novo* or inherited in an autosomal dominant fashion, with the exception of mosaic variegated aneuploidy syndrome (autosomal recessive inheritance).[2]

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 and / or genetic conditions. Genetic counselling is recommended for these families.

Indications for Testing

Patients presenting with features suggestive of one of the below conditions are eligible for testing.

Ordering privileges

This panel may be ordered by Clinical Geneticists.

Pediatric cancer NGS panel

Gene(s)	Associated cancers and/or clinical features[2,3]	Associated Hereditary Syndrome(s)[2,3]
ALK, PHOX2B	Susceptibility to neuroblastoma, increased risk for other cancers	Hereditary neuroblastoma
APC	Colonic polyps, colon cancer, hepatoblastoma	APC-associated polyposis conditions
BUB1B, CEP57	Intrauterine growth restriction, intellectual disabilities, CNS anomalies and cancer predisposition such as Wilms tumor, rhabdomyosarcoma and leukemia	Mosaic variegated aneuploidy syndrome (types 1 & 2)
CDKN1C	Neonatal hypoglycemia, macrosomia, macroglossia, hemihyperplasia, omphalocele, embryonal tumors, visceromegaly, renal anomalies and ear creases / pits	Beckwith-Wiedemann syndrome
	Of note: If a patient is suspected of having BWS, the first line test should be assessment for uniparental disomy of 11p15 or abnormal methylation or deletions of this region, with reflex to CDKN1C sanger sequencing. This testing is available through the Calgary Molecular Genetics Lab.	
DICER1	A tumor susceptibility syndrome that confers an increased risk for pleuropulmonary blastoma (most commonly), ovarian sex cord-stromal tumors, juvenile granulosa cell tumor and thyroid gland neoplasia	DICER1-related disorders
PTCH1, SUFU	Multiple jaw keratocysts and/or basal cell carcinoma, characteristic facial appearance (~60%), skeletal anomalies, medulloblastoma	Nevoid Basal Cell Carcinoma syndrome
SMARCB1	Susceptibility to rhabdoid tumors, onset is typically around 6 months of age	Rhabdoid tumor predisposition syndrome
TP53	Lifetime risk of 68%-93% to develop cancer. The most common tumor types include soft tissue, osteosarcomas, breast cancer and brain cancer	Li-Fraumeni syndrome

WT1	Genital anomalies, cardiac malformations, Wilms tumor and renal disease.	Denys-Drash syndrome Frasier syndrome Meacham syndrome
	Wilms tumor, anirida, genitourinary anomalies, intellectual disability	WAGR
	Susceptibility to Wilms tumor	

Associated Disorders[2,3]
Some of the genes on this panel are associated with other rare disorders including:

Congenital central hypoventilation syndrome (CCHS) is an autosomal recessive disorder caused by pathogenic variants in *PHOX2B*. It is a disorder of respiratory and autonomic regulation and most commonly presents in the newborn period with a classic presentation, however, it can present more mildly at later ages.

Schwannomatosis is an autosomal dominant disorder characterized by multiple schwannomas without the vestibular schwannomas diagnostic of neurofibromatosis type 2. Pathogenic variants in *SMARCB1* are responsible for 30-60% of familial schwannomatosis but only a small percentage of isolated cases.

Pathogenic variants in *PTCH1* have 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
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. National Cancer Institute [Internet]: National Institutes of Health (US). Childhood Cancers. [cited 2022 Sept 1] Available from: https://www.cancer.gov/types/childhood-cancers#:~:text=About%205%20percent%20of%20all,cell%20growth%20and%20eventually%20cancer.

2. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [cited 2022 Sept 1]. Available from: https://medlineplus.gov/;

3. 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/