Pediatric Tumor Panel

Features of Hereditary Pediatric Tumors

Genetic testing with the Pediatric Tumor Panel may be appropriate if you or your child's personal and/or family history is suggestive of a hereditary predisposition to cancer and/or tumors. This includes:

- A personal or family history of cancer diagnosed at a particularly young age (such as rhabdomyosarcoma diagnosed under 3 years of age or thyroid cancer diagnosed in childhood)
- Multiple cancers in one person, either of the same origin (such as multiple brain tumors or bilateral renal tumors) or of different origins (such as medulloblastoma and basal cell carcinoma or adrenocortical carcinoma and sarcoma) with at least one diagnosis in childhood
- A personal or family history of certain cancers and/or benign tumors which are highly associated with a hereditary pediatric tumor syndrome (such as certain pediatric renal tumors or central nervous system tumors)
- Multiple relatives diagnosed with the same or related cancers on the same side of the family and spanning multiple generations

Genes Included on the Pediatric Tumor Panel are Listed in the Table Below

High-Risk Genes Well-studied • Greater than 4-fold risk of developing one or more cancers • Can cause a moderate risk for other cancers • National or expert opinion guidelines for screening and prevention are established

Newer-Risk Genes Not as well-studied • Precise lifetime risks and tumor spectrum not yet determined • Guidelines for screening and prevention are limited or not available

Lifetime Cancer and/or Tumor Risks

	Gene	Lifetime Cancer and/or Tumor Risks*
High-Risk Genes	*ALK*	Neuroblastic tumors (up to 57%)
	APC	Colorectal (up to 93%), Small bowel (4-12%), Gastric, Thyroid, Pancreatic, Brain, Liver, Desmoid tumors, Gastrointestinal polyps
	CDC73	Parathyroid cancer and tumors, Jaw tumors, Renal tumors, Uterine tumors
	EPCAM, MLH1, MSH2, MSH6, PMS2	Colorectal (11-80%), Endometrial (12-71%), Ovarian (1-24%), Gastric (<1-20%), Urinary tract (1-20%), Pancreatic, Biliary tract, Small bowel, Brain, Sebaceous tumors, Prostate For CMMR-D (2 pathogenic variants in the same gene): Brain, Hematologic malignancies, Colon, Small bowel Tumor spectrum is representative of Lynch syndrome; data are limited with regard to the association of certain cancers with pathogenic variants in *MSH6*, *PMS2* and *EPCAM*
	MEN1	Parathyroid tumors (95%), Pancreatic neuroendocrine tumors, Pituitary tumors, Pheochromocytomas and other neuroendocrine tumors
	NF1	Neurofibromas, Brain tumors (2-15%), Pheochromocytomas (1-13%), Sarcomas (6-13%), Female breast, Gastrointestinal stromal tumor (GIST)
	NF2	Schwannomas-vestibular (greater than 90%) and other cranial nerves (24-51%), Central nervous system tumors-spinal tumors (60-90%) and meningioma (50-80%)
	PHOX2B	Neuroblastic tumors (up to 50%)
	PRKAR1A	Myxomas, Testicular tumors (40%), Thyroid (10%), Schwannomas (up to 10%), among others
	PTCH1	Basal cell carcinoma (up to 90%), Brain (5%), Fibromas, Jaw tumors
	PTEN	Female Breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps
	RB1	Retinoblastoma (greater than 90%), Brain (5-10%), Sarcoma-bone and soft tissue, Leukemia, Melanoma
	RET	Thyroid (greater than 90%), Pheochromocytoma (up to 50%), Hyperparathyroidism (up to 30%)
	STK11	Female breast (up to 54%), Colorectal (39%), Pancreatic (11-36%), Gastric (29%), Ovarian tumors (21%), Lung (7-17%), Small bowel (13%), Cervical (10%), Testicular tumors (9%), Endometrial (9%), Gastrointestinal polyps
	TP53	Female breast (85%), Sarcoma-bone and soft tissue, Brain, Hematologic malignancies, Adrenocortical carcinoma, among others. Overall risk for cancer: up to 95% in females, 88% in males
	TSC1, TSC2	Renal cancer (5%) and tumors, Benign central nervous system tumors, Hamartomatous tumors
	VHL	Renal (up to 69%), Pancreatic neuroendocrine tumors (up to 17%), Hemangioblastomas, Pheochromocytomas
	WT1	Wilms tumor (up to 74%)
Newer-Risk Genes	*DICER1*	Lung tumors, Thyroid tumors, Renal tumors, Ovarian tumors, Sarcoma
	SMARCA4	Malignant rhabdoid tumors, Ovarian
	SMARCB1	Malignant rhabdoid tumors, Schwannomas
	SUFU	Brain, Basal cell carcinoma, Meningioma

* Most commonly associated cancer/tumors listed; lifetime risks provided when available. Risks relate to carriers of a single pathogenic variant.

Possible Outcomes of Genetic Testing:

There are four possible outcomes of genetic testing: positive (pathogenic variant), likely pathogenic variant, variant of uncertain significance (VUS), and negative. Genetic counseling is recommended prior to genetic testing to understand the benefits and limitations of testing.

A positive result indicates a genetic variant (change) was identified in a specific gene and that variant is pathogenic (harmful). With a positive test result, the risk to develop a particular disease (in this case, cancer and/or tumors) is increased.

A likely pathogenic variant result indicates that there is a variant in a specific gene for which there is significant, but not conclusive, evidence of an increased risk to develop a particular disease (in this case, cancer and/or tumors).

A variant of uncertain significance (VUS) result means that a change in a specific gene was identified, however the effect of the variant cannot be clearly established. There may be conflicting or incomplete information in the medical literature about this variant and its association with an increased risk of cancers and/or tumors is unknown. In other words, it cannot be determined yet whether this variant is associated with an increased risk of cancer and/or tumors or it is a harmless (normal) variant.

A negative result means that no reportable changes were identified.

Medical Management Based on Genetic Test Results

Clinical guidelines may be available which provide options and recommendations for patients who have a positive (pathogenic variant) test result indicating an increased risk for cancer and/or tumors. Guidelines and recommendations for early detection and/or risk reduction are specific to the gene in which the pathogenic variant was found.

Recommendations may include:

- Blood or urine analysis
- Imaging exams, such as a MRI, CT and/or ultrasound
- Clinical exams, such as dental, skin, hearing or eye exams
- Risk-reducing surgery

If you or your child has a positive or a likely pathogenic variant result, the test report will include additional information regarding available medical management options.

If you or your child has a negative or a variant of uncertain significance (VUS) test result, medical management should be based upon your personal and/or family history of cancer and/or tumors.

Once your test results are available, a discussion with your healthcare provider is recommended to determine the most appropriate medical management options for you and your family.

Regardless of the test results, consider sharing them with family members so that they may discuss the results with their healthcare providers. If you or your child has a positive or a likely pathogenic variant result, family members are at risk to have the same variant and should consider genetic testing to best understand their chance of developing cancer and/or tumors.

Resources

General

American Cancer Society
www.cancer.org/cancer/cancerinchildren

GeneDx
www.genedx.com/oncology

National Cancer Institute
www.cancer.gov

Pediatric Resources

Children's Oncology Group
www.childrensoncologygroup.org

CureSearch
www.curesearch.org

Find a Genetic Counselor

Canadian Association of Genetic Counsellors
www.cagc-accg.ca

National Society of Genetic Counselors
www.nsgc.org

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