Brain Tumor Panel

Features of Hereditary Brain Tumor

Genetic testing with the Brain 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 a brain tumor highly associated with a hereditary syndrome (such as atypical teratoid/rhabdoid tumor (AT/RT), choroid plexus carcinoma, hemangioblastoma, Lhermitte-Duclos Disease, optic glioma, subependymal giant cell astrocytoma (SEGA), or clear cell meningioma)
- A personal or family history of a brain tumor diagnosed at a young age (i.e. ≤18 years) along with additional features of a hereditary syndrome (such as café-au-lait macules, macrocephaly, and hyperparathyroidism among others)
- Multiple tumors and/or cancers in one person, either of the same origin (such as multiple primary brain tumors) or of different origins (such as astrocytoma and melanoma or medulloblastoma and basal cell carcinoma)
- Multiple relatives diagnosed with brain tumors and/or related cancers on the same side of the family and spanning multiple generations

Genes Included on the Brain 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

Current Lifetime Cancer and/or Tumor Risks

	Gene	Lifetime Cancer and/or Tumor Risks*
High-Risk Genes	*APC*	Colorectal (up to 93%), Duodenal or periampullary (4-12%), Gastric, Thyroid (up to 3%), Pancreatic, Brain-medulloblastoma, Liver-hepatoblastoma, Desmoid tumors, Gastrointestinal polyps
	CDKN2A	Melanoma (28-76%), Pancreatic (14%), Brain-astrocytoma
	EPCAM	Colorectal (69-75%), Endometrial (12-55%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	MEN1	Hyperparathyroidism, Parathyroid tumors (95%), Pancreatic neuroendocrine tumors, Pituitary tumors, Ependymoma, Meningioma, Pheochromocytomas and other neuroendocrine tumors
	MLH1	Colorectal (22-80%), Endometrial (31-54%), Ovarian (13-20%),Gastric (6-20%), Urinary tract-transitional cell (1-3%), Pancreatic (1-4%), Biliary tract (2%), Small bowel, Brain, Sebaceous neoplasms, Prostate
	MSH2	Colorectal (22-80%), Endometrial (31-61%), Ovarian (10-24%), Urinary tract-transitional cell (8-20%), Gastric (<1-9%), Pancreatic (1-4%), Biliary tract, Small bowel (1%), Brain, Sebaceous neoplasms, Prostate
	MSH6	Colorectal (20-44%), Endometrial (16-71%), Ovarian (1-11%), Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	NF1	Neurofibromas, Optic nerve gliomas (15%), Pheochromocytomas (1-13%), Malignant peripheral nerve sheath tumors (6-16%), Brain tumors (2-3%), 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%)
	PMS2	Colorectal (11-20%), Endometrial (12-15%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	PTCH1	Basal cell carcinoma (up to 90%), Brain-medulloblastoma, Fibromas-cardiac and ovarian, Jaw tumors-odontogenic keratocysts, Meningioma
	PTEN	Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps, Lhermitte-Duclos disease
	TP53	Female breast (85%), Soft tissue sarcoma, Osteosarcoma, Brain, Hematologic malignancies-Acute leukemias among others, 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-subependymal nodules and subependymal giant cell astrocytomas, Hamartomatous tumors-cardiac rhabdomyomas and angiomyolipomas
	VHL	Renal-clear cell (up to 69%), Hemangioblastomas-retinal and central nervous system (50-80%), Pheochromocytomas (11-19%), Pancreatic neuroendocrine tumors (8-17%), Endolymphatic sac tumors (up to 10%)
Newer-Risk Genes	*CDKN1B*	Hyperparathyroidism, Pituitary tumors, Gastro-entero-pancreatic neuroendocrine tumors, Parathyroid tumors
	DICER1	Lung tumors-pleuropulmonary blastoma, Thyroid tumors-multinodular thyroid goiter and cancer, Renal tumors-cystic nephroma, Ovarian tumors-Sertoli-Leydig, Embryonal rhabdomyosarcoma-cervix, Pituitary blastoma, Pineoblastoma, among others
	POT1	Melanoma, Brain-glioma
	SMARCA4	Malignant rhabdoid tumors-atypical teratoid/rhabdoid tumor of the brain and malignant rhabdoid tumors of the kidney, Ovarian-small cell carcinoma of the ovary, hypercalcemic type

Please see reverse side for remainder of Newer-Risk genes

Newer-Risk Genes	*SMARCB1*	Malignant rhabdoid tumors-atypical teratoid/rhabdoid tumor of the brain and malignant rhabdoid tumors of the kidney, Schwannomas, Meningiomas
	SMARCE1	Meningiomas clear cell type-cranial and spinal
	SUFU	Brain-medulloblastoma, 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:

- Clinical exams, such as skin or eye exams
- Blood or urine analysis
- Imaging exams, such as a mammogram, MRI, CT and/or ultrasound
- Screening procedures, such as a colonoscopy or endoscopy
- Risk-reducing medications or 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

Brain Tumor Resources

American Brain Tumor Association
www.abta.org

National Brain Tumor Society
www.braintumor.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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Information current as of 08/2018