Brain Tumor Panel

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OPKO Health Companies

Hereditary Brain Tumors

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 (see table below) on the same side of the family and spanning multiple generations

Your healthcare provider will determine if genetic testing is medically necessary for you.

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

	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 (28-67%), Pancreatic (17%), 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%), Neuroendocrine tumors of the gastro-entero-pancreatic (GEP) tract (up to 80%), Anterior pituitary tumors (20-65%), Carcinoid tumors, Adrenal tumors (pheochromocytomas and adrenocortical tumors), and other tumors
	MLH1	Colorectal (34-46%), Endometrial (18-54%), Ovarian (10-20%), Gastric (6-20%), Urinary tract-transitional cell (1-4%), Pancreatic (1-4%), Biliary tract (2-3%), Small bowel (4-12%), Brain, Sebaceous neoplasms, Prostate
	MSH2	Colorectal (37-48%), Endometrial (21-57%), 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 (1-13%), 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 (up to 26%), 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 (12-26%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	PTCH1	Basal cell carcinoma (up to 90%), Brain-medulloblastoma (~2%), 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	Renal cancer (5%) and tumors, Benign central nervous system tumors-subependymal nodules and subependymal giant cell astrocytomas, Hamartomatous tumors-cardiac rhabdomyomas and angiomyolipomas
	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%)

	Gene	Lifetime Cancer and/or Tumor Risks*
Newer 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
	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
	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.
**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*.

Possible Outcomes of Genetic Testing

+ Positive

- Pathogenic or likely pathogenic variant identified
- Medical management recommendations may be available
- Family member testing may be recommended

− Negative

- No significant genetic changes identified
- Medical management based on personal and/or family history

? Variant of Uncertain Significance (VUS)

- A genetic change identified, but its association with disease is unclear
- Medical management based on personal and/or family history

Medical Management Based on Genetic Test Results

Clinical guidelines may be available which provide options and recommendations for patients who have a positive (pathogenic or likely 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 dental, skin, hearing 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

In some cases, guidelines for screening and prevention are limited or not available for a positive result. 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.

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