Rhabdoid tumour predisposition syndrome 1 (RTPS-1) is a cancer syndrome that predisposes an individual to rhabdoid tumours. These tumours are referred to as atypical teratoid/rhabdoid tumours (AT/RT) when arising in the central nervous system, and as malignant rhabdoid tumours (MRTs) if found in other sites (i.e. renal, liver, lung, skin, heart). Most of these tumours are characterized by loss of function of the SMARCB1 gene. Germline mutations in SMARCB1 can predispose an individual to developing these tumours. Rhabdoid tumours are highly malignant and usually occur in children less than 2 years of age, and may present in multiple sites.

Schwannomatosis is a genetic condition characterized by multiple schwannomas. Schwannomas can arise wherever Schwann cells occur, in the spinal cord and along peripheral and cranial nerves. The most common presentation of non-vestibular nerve schwannomas is painful lumps along the skin and/or neurological deficits.

**GENETICS**

RTPS-1 and schwannomatosis are caused by heterozygous germline mutations in the SMARCB1 gene, located on chromosome 22 (22q11.2). These conditions are inherited in an autosomal dominant manner, meaning that the disease will be present when a person has one mutated copy of the SMARCB1 gene. Both conditions show variability in ages of onset, sites of tumour development, and severity. However, most patients with RTPS-1 due to germline SMARCB1 mutations are very young (median age 5 months) and present more often with multisite disease compared with 18 months for sporadic mutations.

Cases of gonadal mosaicism (multiple affected children of an unaffected parent) have been reported. Germline SMARCB1 mutations may show variable penetrance, where parents of affected children that have SMARCB1 mutations may develop schwannomatosis later in life or may stay asymptomatic. RTPS-1 and schwannomatosis can both be de novo (caused by new mutations that are not inherited). The risk of developing tumors or schwannomatosis when a germline mutation is found is unknown.

**WHO SHOULD BE TESTED?**

- Individuals with a rhabdoid tumour or clinically suspected of being affected with schwannomatosis,
- Unaffected relatives of individuals with a rhabdoid tumour or schwannomatosis
- Pregnancies at risk due to a family history of rhabdoid tumours or schwannomatosis, if familial mutation is known.

**TEST METHODS**

- Complete sequencing of the 9 exon coding regions and flanking exon/intron boundaries of the SMARCB1 gene to identify point mutations on genomic DNA
- Quantitative testing of the SMARCB1 to test for deletions or duplications, using Multiplex Ligation-dependent Probe Amplification (MLPA) on genomic DNA

**TEST SENSITIVITY**

- Germline mutations in SMARCB1 are found in 35–50% of children diagnosed with rhabdoid tumours but is seen at higher frequency (up to 60%) in younger children affected with rhabdoid tumours (<6months at diagnosis)
- Germline mutations in SMARCB1 are estimated to contribute to ~10% of sporadic and ~85% of familial schwannomatosis.

**BEFORE MOLECULAR TESTING**

Immunohistochemical staining for the SMARCB1 protein in tumour cells is required. If the results are negative (no protein found) molecular testing is warranted.

**For More Information**

Online Mendelian Inheritance In Man:

Children’s Tumor Foundation: http://www.ctf.org/Living-with-NF/schwannomatosis.html

Malignant Rhabdoid Tumors: http://emedicine.medscape.com/article/993084-overview

To locate a genetics center near you, please visit the Canadian Association of Genetic Counselors website at www.cagc-acgg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility of inherited form of rhabdoid tumour predisposition syndrome.
2. The clinical course or severity of symptoms cannot be predicted by molecular analysis.
3. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.
4. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.