Mass General Brigham
Mass General Cancer Center

What you need to know

RET Gene

What does it mean to have a *RET* pathogenic variant?
Having a *RET* pathogenic variant, also known as a mutation, means a person has a version of the *RET* gene that does not work properly. This causes a condition known as Multiple Endocrine Neoplasia Type 2 (MEN2) syndrome. There are two subtypes of this syndrome: MEN2A and MEN2B.

Pathogenic variants in the *RET* gene can also cause a different genetic disease known as Hirschsprung disease, which is diagnosed in infancy. Individuals with MEN2 rarely develop Hirschsprung disease.

What is my risk for cancers or tumors if I have a *RET* pathogenic variant?
If you have a *RET* pathogenic variant, you have a greater risk of developing certain types of cancers and benign tumors of the endocrine system. The endocrine system is made up of endocrine glands, which secrete hormones to control important functions in the body such as mood, growth and development, and metabolism.

Benign tumors are not cancerous and do not spread, whereas cancerous (also called malignant) tumors can spread to nearby healthy tissue and organs. Cancerous tumor cells also have the potential to spread (metastasize) to other more distant sites of the body. Benign and malignant tumors are often treated in different ways.

Lifetime Tumor and Cancer Risks

	MEN2A	MEN2B
Medullary thyroid cancer	≤ 98%*	≤ 98%*
Pheochromocytoma (benign adrenal gland tumor)	≤ 50%	≤ 50%
Primary hyperparathyroidism (parathyroid adenoma)	≤ 25%	Not increased

NCCN: Neuroendocrine and Adrenal Tumors, v.2.2022
*Emerging data suggest that the risk for medullary thyroid cancer can be significantly lower in some families.

Individuals with MEN2B will generally have a tall slim body type, hyperflexible joints and scoliosis. Some families with *RET* pathogenic variants may also develop benign tumors of the gastrointestinal tract (ganglioneuromas), lips, and tongue (mucosal neuromas).

If I have a *RET* pathogenic variant, what is the chance my family members will have it too?
There is a 50% chance that a person with a pathogenic variant will pass it on to each of their children. In most cases, siblings of a person with a pathogenic variant have a 50% chance to have the pathogenic variant. Additionally, other family members are at risk to have the pathogenic variant.