Ambry Genetics®

Understanding Your Positive *RET* Genetic Test Result

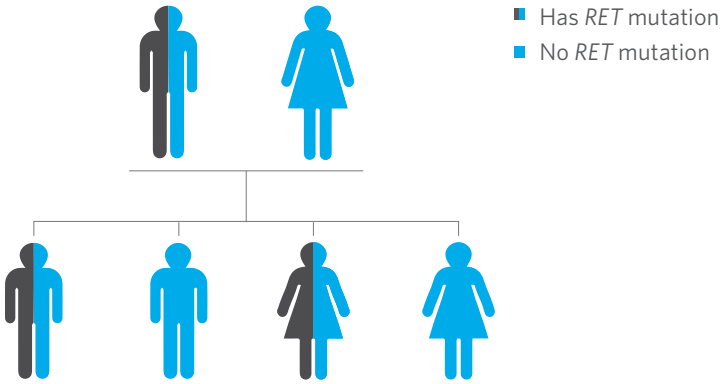
INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION** OR **VARIANT, LIKELY PATHOGENIC**

5 THINGS TO KNOW

1	*RET* mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the *RET* gene.
2	Multiple endocrine neoplasia type 2	People with *RET* mutations have multiple endocrine neoplasia type 2 (MEN2).
3	Non-cancerous tumor and cancer risks	You have an increased chance to develop medullary thyroid cancer, pheochromocytomas (PCCs), possibly hyperparathyroidism, and other non-cancerous tumors or medical concerns.
4	What you can do	There are risk management options to detect cancer early or lower your risk to develop cancer. It is important to discuss these options with your doctor, and decide on a plan that best manages your cancer risks.
5	Family	Family members may also be at risk – they can be tested for the *RET* mutation that was found in you.

RET MUTATIONS IN THE FAMILY

There is a 50/50 random chance to pass on an *RET* mutation to your sons and daughters. The image to the right shows that both men and women can carry and pass on these mutations.



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RESULT	MUTATION	Your testing shows that you have a pathogenic mutation (a disease-causing change in the gene, like a spelling mistake) or variant that is likely pathogenic in the *RET* gene. Both of these results should be considered positive.
GENE	*RET*	Everyone has two copies of the *RET* gene, which we randomly inherit from each of our parents. Mutations in one copy of the *RET* gene can increase the chance for you to develop certain types of cancer in your lifetime.
CONDITION	MEN2	People with *RET* mutations have multiple endocrine neoplasia type 2 (MEN2). MEN2 can be divided into three subtypes: MEN2A, MEN2B, and familial medullary thyroid carcinoma (FMTC).
TUMOR/CANCER RISKS	INCREASED	You have an increased risk for cancerous and non-cancerous tumors depending on the specific *RET* mutation you have: • MEN2A: medullary thyroid cancer (95-100%), PCCs (up to 50%), and hyperparathyroidism (up to 30%) • MEN2B: medullary thyroid cancer (95-100%), PCCs (up to 50%). Additional risks for tumors in the mouth, eyes, GI tract, and lungs. • FMTC: medullary thyroid cancer only (95-100%) The specific *RET* gene mutation you have will determine which subtype you have, and may provide you more information about your specific tumor/cancer risks. Talk to your doctor about which tumors and cancers you are at risk for.
OTHER MEDICAL CONCERNS	MAY BE PRESENT	Depending on the type of *RET* gene mutation you have, you could have an increased risk for Hirschprung disease (a non-cancerous condition that affects the colon) in addition to/instead of the tumor/cancer risks mentioned above.
MANAGEMENT OPTIONS	 FOR MEN & WOMEN	Options for prophylactic thyroidectomy, screening, and early detection may begin very early in childhood and may include a thorough annual physical exam including imaging, such as ultrasounds, CT scans, or MRIs, as well as blood screening tests. Talk to your doctor about when to begin screening and which options may be right for you.
RISK MANAGEMENT	VARIES	Risk management decisions are very personal, and the best option depends on many factors. Screening typically begins earlier than in the general population, and is often more frequently done. It is important to discuss these options with your doctor.
FAMILY MEMBERS	50/50 CHANCE	Your close relatives (like your parents, brothers, sisters, children) have a 50/50 random chance of inheriting the *RET* mutation that you carry, and other family members (like your aunts, uncles, cousins) may also inherit it. Your relatives can be tested for this same mutation. Depending on the family history, those who DO NOT have it may not have an increased lifetime chance (above the general population) to develop cancer.
NEXT STEPS	DISCUSS	It is recommended that you share this information with family members so they can learn more and discuss this with their healthcare providers.
REACH OUT	RESOURCES	• Association for Multiple Endocrine Neoplasia Disorders (AMEND) amend.org.uk • Thyca: Thyroid Cancer Survivors' Association thyca.org • Genetic Information Nondiscrimination Act (GINA) ginahelp.org • National Society of Genetic Counselors nsgc.org • Canadian Society of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *RET* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

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