Researchers discover new thyroid cancer gene

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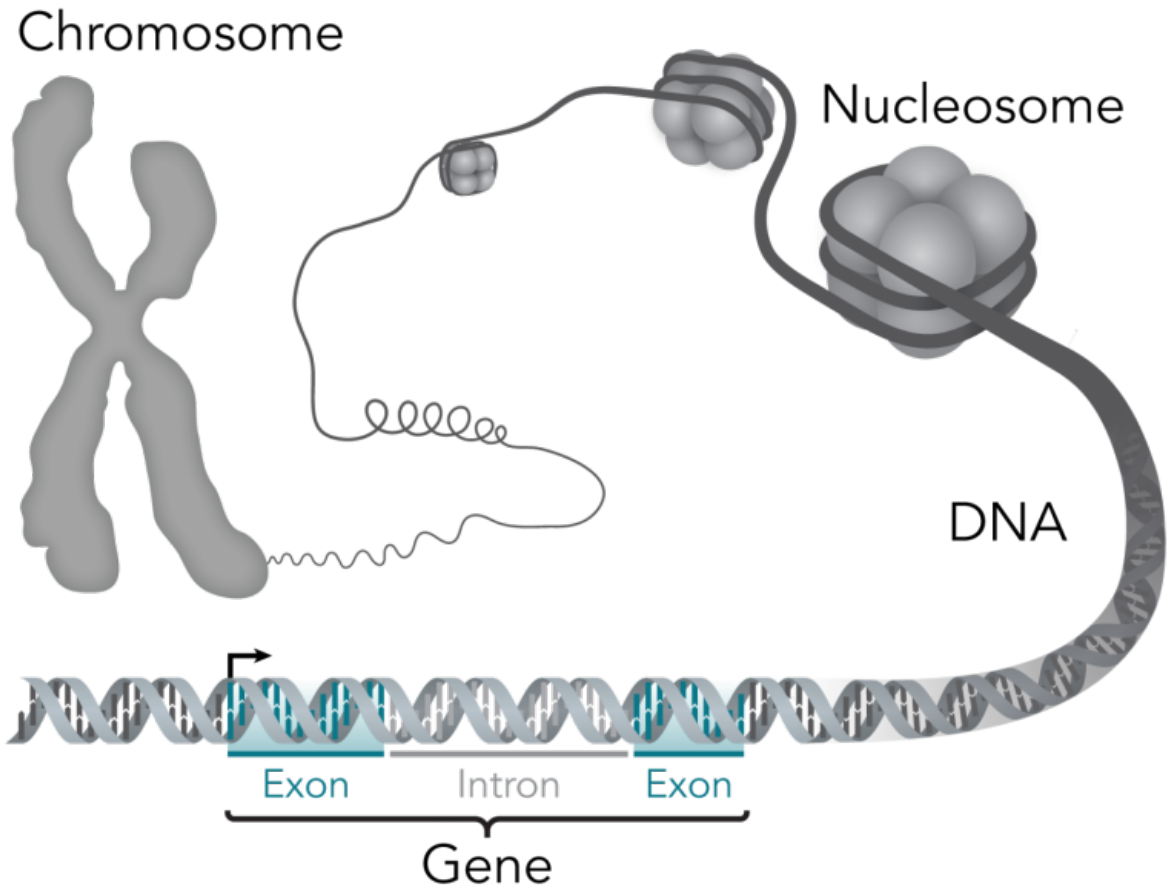

This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only the exons encode the protein. The diagram labels a region of only 55 or so bases as a gene. In reality, most genes are hundreds of times longer. Credit: Thomas Splettstoesser/Wikipedia/CC BY-SA 4.0

Cleveland Clinic researchers have discovered a new gene associated with Cowden syndrome, an inherited condition that carries high risks of thyroid, breast, and other cancers, and a subset of non-inherited thyroid cancers, as published today in the online version of the *American Journal of Human Genetics*.

Thyroid cancer, the most common cancer of the endocrine glands, is the fastest rising cancer in women and second fastest rising in men in the U.S. The new gene, SEC23B, discovered by Charis Eng, MD, PhD, Founding Chair of the Genomic Medicine Institute within Cleveland Clinic's Lerner Research Institute and Director of the Center for Personalized Genetic Healthcare, encodes a protein involved in the transport of all proteins within cells.

Dr. Eng and her team started their gene-hunting journey 3 years ago by examining a multi-generational family with early-onset thyroid cancers. They found that all affected family members had inherited a harmful mutation in this gene. The mutation was not found in any unaffected family members.

"This isn't the first time we discovered novel genetic mutations in Cowden syndrome," said Dr. Eng, "but what was truly remarkable is that the SEC23B gene had been identified back in 2009 as the cause of a very rare type of anemia, but not cancer."

In contrast to anemia, where SEC23B function is lost, Dr. Eng and her team discovered that normal thyroid cells expressing mutated SEC23B grew faster, formed larger colonies, invaded more aggressively, and were able to survive in a very stressful microenvironment—all major hallmarks of cancer.

"Our data not only identified a novel cancer-predisposing gene, particularly in thyroid cancer, but also highlighted how cellular stress responses can be hijacked by cancer cells to promote their survival," said Dr. Eng.

Further analyses uncovered that SEC23B mutations are present in up to 3 percent of unrelated Cowden syndrome patients and in 4 percent of patients with non-syndromic thyroid cancer. With up to 50 percent of Cowden syndrome patients testing negative for all known genetic mutations, the syndrome remains an under-diagnosed and difficult-to-recognize condition.

"The discovery of this new cancer-predisposing gene will facilitate predictive genetic testing, risk assessment, genetic counseling, and clinical management of the disease," said Dr. Eng.

Patients with Cowden syndrome develop noncancerous growths, called hamartomas, that can appear on the skin, in mucous membranes and in the intestinal tract. Cowden syndrome predisposes individuals to several types of cancers - an 85 percent lifetime risk of breast cancer, a 35 percent risk for epithelial thyroid cancer, and increased risks of uterine, kidney and colon cancers as well. At least one in 200,000 people are affected by the disease.

Dr. Eng previously discovered that Cowden syndrome is caused by a faulty tumor suppressor gene called PTEN (phosphatase and tensin homolog). The gene has since been implicated in a number of other conditions, including a rare form of autism.

Provided by Cleveland Clinic