TGen study identifies gene fusion as likely cause of rare type of thyroid cancer

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In a scientific first, the fusion of two genes, ALK and EML4, has been identified as the genetic driver in an aggressive type of thyroid cancer, according to a study by the Translational Genomics Research Institute (TGen).

These groundbreaking findings are based on genetic sequencing of tumor cells from a 62-year-old patient with an aggressive tall cell variant of papillary thyroid cancer, according to the study published Tuesday, March 18, in the *World Journal of Surgery*, the official journal of the International Society of Surgery.

The patient's thyroid cancer recurred after he had undergone multiple operations, external beam radiation and chemotherapy, and so the patient appeared to be a candidate for additional study.

Following one surgery in June 2011, a sample of the patient's tumor was obtained and studied by whole-genome sequencing, in which TGen spells out, in order, the more than 3 billion chemical base pairs that make up human DNA.

A comparison of the tumor DNA to the patient's normal DNA found 57 mutations in 55 genes of the cancer genome. The investigators also found a rearrangement between two genes. This translocation and fusion of EML4-ALK was identified as the genetic driver of the patient's cancer.

"This is the first report of the whole genome sequencing of a papillary thyroid cancer, in which we identified an EML4-ALK translocation. This is important because we have a drug that can target this fusion and treat the patient," said Dr. Michael J. Demeure, Clinical Professor and Director of TGen's Rare Cancer Unit, and the study's principal investigator and lead author. "This patient's tumor did not harbor more well-known gene mutations that are associated with most thyroid cancers. These findings suggest that this tumor has a distinct oncogenesis, or the genetic cause of cancer."

There are few therapeutic options for patients with radioiodine-resistant aggressive papillary thyroid cancer. The EML4-ALK fusion appears in about 5 percent of lung cancers, which are usually treated with a targeted drug known as crizotinib.

By identifying the EML4-ALK fusion in this study, TGen was able to recommend crizotinib for this study's 62-year-old patient, whose cancer then remained progression-free for more than 6 months.

"Whole-genome sequencing technologies offer the promise of allowing for precision targeted treatment for human diseases, including cancer," said Dr. John Carpten, TGen Deputy Director of Basic Science, and Director of TGen's Integrated Cancer Genomics Division, and the study's senior author. "Through a greater understanding of the molecular oncogenesis of a specific cancer, one would hope to devise more effective, individualized treatments."

Whole genome sequencing is particularly beneficial for patients with relatively rare tumors, since they generally have less access to new drug treatments often available through clinical trials, according to the study, Whole-genome sequencing of an aggressive BRAF wild-type papillary thyroid cancer identified EML4-ALK translocation as a therapeutic target.

Also contributing to this study were physicians from Arizona Oncology, and Scottsdale Pathology Consultants.

Provided by The Translational Genomics Research Institute