ONCOLOGY TIMES

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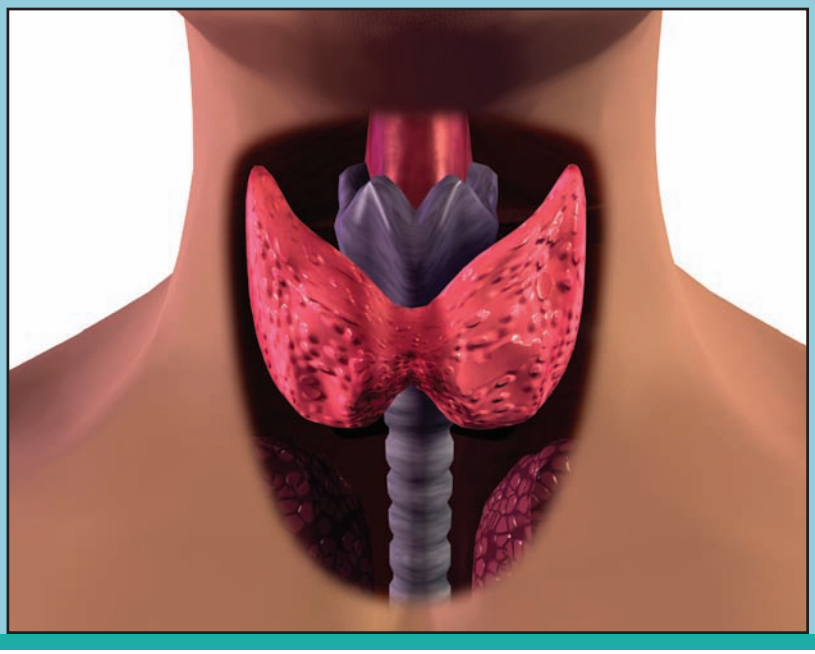
Independent News on
HEMATOLOGY / ONCOLOGY

SPECIAL EDITION Supplement to May 25, 2014 issue



Vol. 2, #3

# FOCUS: Thyroid Cancer

*Treatment & Research Updates*

## [INSIDE]

# ALK and EML4 Genes Shown as Likely Cause of Rare Type of Aggressive Papillary Thyroid Cancer

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 researchers at the Translational Genomics Research Institute (TGen).

The findings were based on genetic sequencing of tumor cells from a 62-year-old patient with the aggressive tall cell variant of papillary thyroid cancer, according to the study, now available online ahead of print in *World Journal of Surgery (DOI 10.1007/s00268-014-2485-3)*.

The patient's thyroid cancer had recurred after he had had several surgeries, external-beam radiation therapy, and treatment with sorafenib.

Following one surgery in June 2011, a tumor sample was obtained and studied by whole genome sequencing. A comparison of the tumor DNA with the patient's normal DNA found 57 mutations in 55 genes of the cancer genome as well as rearrangement between two genes—it was this translocation and fusion of EML4-ALK that 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," the study's lead author, Michael J. Demeure, MD, Clinical Professor and Director of TGen's Rare Cancer Unit, said in a news release.

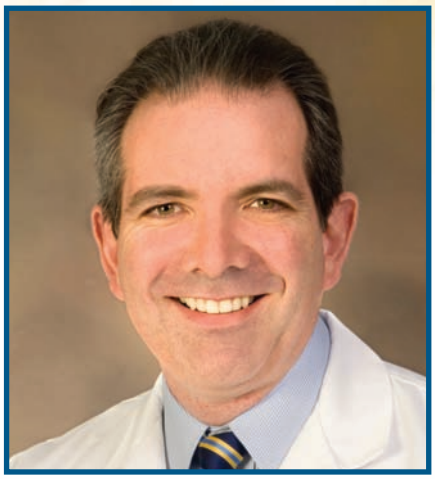
"This is important because we have a drug that can target this fusion and treat the patient. This patient's tumor did not harbor more well-known gene mutations that are associated with most thyroid cancers. These findings suggest that this tumor has a distinct oncogenesis."

There are few therapeutic options for patients with radioiodine-resistant aggressive papillary thyroid cancer. The EML4-ALK fusion appears in about five percent of lung cancers, which are usually treated with crizotinib. Once EML4-ALK fusion was found for this thyroid cancer patient, the researchers were able to recommend that he be treated with crizotinib, and he then remained progression-free for more than six months, the study noted.

The researchers wrote that the prevalence of such genomic aberrations in papillary thyroid cancer is not known, but should be discernible by screening larger sample sets using techniques that are less expensive and labor intensive than whole genome sequencing, such as fluorescence in situ hybridization, immunohistochemistry, or reverse-transcription polymerase chain reaction.

Whole genome sequencing is not yet practical for routine clinical use, the article said, but it can be particularly helpful in the case of relatively rare tumors where clinical trials in which large groups of patients comparing encouraging new treatments to standard treatments are difficult to conduct.

"The promise of using whole genome sequencing to cure cancer is still just that: a promise that offers hope for the future. The field needs a better understanding of the interactions between oncogenic pathways and then ways to develop additional agents to more effectively treat tumors with less toxicity. Then, perhaps, the promise of personalized precision treatment for aggressive thyroid cancers may be fulfilled."



MICHAEL J. DEMEURE, MD: "This is the first report of the whole genome sequencing of a papillary thyroid cancer, in which we identified an EML4-ALK translocation—important because we have a drug that can target this fusion, and the tumor did not harbor more well-known gene mutations associated with most thyroid cancers."

Other coauthors of the study were Meraj Aziz of TGen, Richard Rosenberg of Arizona Oncology, Steven D. Gurley of Scottsdale Pathology Consultants, Kimberly J. Bussey of TGen, and John Carpten, TGen's Deputy Director of Basic Science and Director of the Integrated Cancer Genomics Division.

## Coming Soon!

- Threefold Increased Cardiovascular Mortality Found in DTC Patients
- Hints from Large Prospective Study that Taller, Heavier Children May Have Higher Risk of Adult Thyroid Cancer
- Death Rate Higher for Younger Patients with Secondary Thyroid Cancers