Study Paves Path to Improved Diagnosis, Treatment of NUT Carcinoma

Dana-Farber research uncovered the potential for underdiagnosis of this aggressive lung, head and neck cancer and identified additional tests required for an accurate diagnosis.

July 28, 2025 By Dana-Farber Cancer Institute

The diagnosis of a suspected lung, head, and neck cancer called NUT carcinoma should include additional testing capable of detecting gene fusions that are definitive markers of the disease, according to a study by Dana-Farber Cancer Institute investigators. The study showed that more than 75 percent of patients with NUT carcinoma may not be immediately diagnosed because standard-of-care DNA testing does not detect NUT carcinoma fusion genes.

Tests that can identify gene fusions that are specific to NUT carcinoma include NUT immunohistochemistry (IHC), RNA fusion testing, and NUTM1 FISH (fluorescence in situ hybridization).

The findings were published in Clinical Cancer Research.

“If a diagnosis of NUT carcinoma is being considered, standard of care DNA-based testing is insufficient and clinicians should consult with pathology colleagues about ordering a better gold standard test such as NUT immunohistochemistry or RNA-based mutation sequencing,” says co-senior author Dr. Jia Luo, a thoracic oncologist at the Lowe Center for Thoracic Oncology at Dana-Farber. “Early accurate diagnosis is key to getting patients on the correct treatment and clinical trials.”

NUT carcinoma is an aggressive squamous cell cancer. A patient might be suspected of having NUT carcinoma if they are young, have little to no history of smoking, and have a poorly differentiated cancer in the lungs, head, or neck. Median survival for patients with NUT carcinoma is 6.7 months.

NUT carcinoma is defined by fusions of the NUTM1 gene with other genes. Gene fusions occur when errors in the genome glue two genes together, resulting in the production of a malfunctioning protein.

Luo and co-senior author Christopher French, MD, of Brigham and Women's Hospital, initiated the study to determine the best means of detecting these gene fusions and definitively diagnosing NUT carcinoma. They examined the diagnostic results of 116 NUT carcinoma tumors that had undergone molecular testing using a range of panel tests including next-generation DNA sequencing, circulating tumor DNA (ctDNA) testing, and tests that identify gene fusions.

They found that DNA sequencing and ctDNA testing detected NUT fusions less than 25 percent of the time. In contrast, NUT IHC, RNA fusion testing, and NUTM1 FISH testing detected NUT carcinoma fusions much more reliably, respectively 100 percent, 84 percent and 92 percent of the time.

"These findings warrant immediate change to the diagnostic workflow for patients with suspected NUT carcinoma," says Luo. This approach of performing DNA testing and RNA fusion testing simultaneously is used in other cancers in which the identification of gene fusion is needed to make a diagnosis.

The study also took an inventory of other mutations detected by the tests in the NUT carcinoma cases. More than half of the cases did not contain a second cancer-associated gene mutation, but some did.

Those that did contain additional gene mutations turned out to be genes associated with epigenetic, cell cycle and DNA repair pathways. Luo and colleagues are initiating laboratory studies to determine if targeting these mutations could benefit patients.

"This study characterized the common mutations seen in NUT carcinoma, which will help researchers develop future effective combination treatments," says Luo.

Funding: National Institutes of Health, Dana-Farber/Harvard Cancer Center Lung Spore Career Enhancement Program, American-Italian Cancer Foundation Post-Doctoral Research Fellowship, Lowe Center for Thoracic Oncology, Friends of Jay Dion, the Ryan Richards Foundation, McDevitt Strong, the Max Vincze Foundation, the Victor Family Foundation, the Fortisure Foundation for NUT Carcinoma Research, and the Alexandra Hallock Memorial Fund.

This news release was originally published July 24, 2025, by Dana-Farber Cancer Institute. It is republished with permission.
