Blood mutations could contaminate genetic analyses of tumors

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Genetic mutations in blood cells that have made their way into tumors could be red herrings that mislead physicians looking for genetic changes in tumors that are helping to drive the cancer. This finding is significant because physicians could make misinformed treatment decisions.

At the 2018 American Society of Clinical Oncology Annual Meeting this week, University of North Carolina Lineberger Comprehensive Cancer Center researchers and colleagues reported that blood cell mutations accounted for as many as 8 percent of the mutations identified in large-scale genetic sequencing efforts at two major academic centers. The findings were also published in the journal *Clinical Cancer Research*.

"Next-generation sequencing of solid tumors is intended to identify acquired mutations within tumor tissue," said the study's first author Catherine C. Coombs, an associate member of UNC Lineberger and an assistant professor of medicine in the division of hematology/oncology. "The identification of acquired mutations in blood cells could lead to errors in interpretation of sequencing results."

For the study, researchers reviewed data from patients with solid tumor cancers who had genetic sequencing tests performed by Foundation Medicine as part of their routine clinical care at the N.C. Cancer Hospital and the Moffitt Cancer Center between 2013 and 2017. They also analyzed sequencing results for blood samples. A subset of patients at the N.C. Cancer Hospital had their tumors and their blood sequenced through UNCseq, a genetic sequencing clinical trial run by UNC Lineberger researchers. For patients at Moffitt Cancer Center, they compared Foundation Medicine results to sequencing results from banked blood samples.

The researchers analyzed the data to identify mutations more commonly seen in blood cells. They found that "clonal hematopoiesis," which are acquired mutations in blood cells, accounted for 8 percent of the mutations.

"The presence of clonal hematopoiesis mutations on next-generation sequencing reports from solid tumor biopsies can confound assay interpretation with the risk of misguided application of targeted therapies," Coombs said.

Researchers say further work must be done to develop standard processes for differentiating mutations that occur in the blood versus the tumor in order to ensure accuracy in the tests for physicians who are using the sequencing results to choose personalized treatments for patients. In addition, the study shows an advantage to "paired" sequencing tests, which evaluate mutations in both the blood and the tumor.

"It adds expense, but it can be useful in determining whether a suspicious mutation is blood-derived, or tumor-derived," Coombs said.

More information: Catherine C. Coombs et al. Identification of clonal hematopoiesis mutations in solid tumor patients undergoing unpaired next-generation sequencing assays, *Clinical Cancer Research* (2018). DOI: 10.1158/1078-0432.CCR-18-1201

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