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Can Chemotherapy Cause Cancer Relapse?

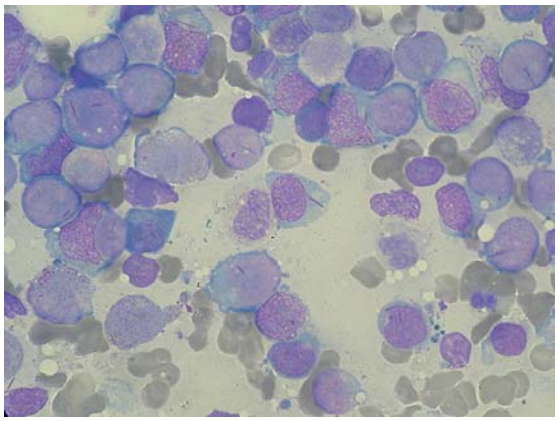
Chemotherapy is necessary for saving the lives of many cancer patients, but can it also contribute to the cancer's recurrence? A study published online this month in *Nature* used deep sequencing to track how cancer genomes evolve after chemotherapy in patients with acute myeloid leukemia (AML) and revealed evidence that chemotherapy leads to new mutations.

Although chemotherapy is effective at putting cancer into remission for most patients with AML, the majority eventually experience a relapse. A longstanding question concerns the extent to which chemotherapy itself contributes to relapses by driving mutations that allow cancer cells to resist treatment.

To better understand how chemotherapy affects the cancer genome, researchers at Washington University School of Medicine in St. Louis, MO, sequenced the genomes of primary tumors from 8 patients with AML who had undergone chemotherapy but eventually experienced a relapse.

Comparing the genetic sequences in skin and initial and relapsed tumor samples with a median of 590-fold coverage per site, the researchers tracked the evolution of distinct clusters of cancer cells with the same mutations. They found that, in all cases, patients had a founding clone that was the basis for AML, and that the founding clone or a subclone derived from it gained mutations that allowed it to survive and evolve into the relapse clone.

John DiPersio, MD, PhD, a medical oncologist and senior author of the article, says that, whereas chemotherapy was associated with new mutations, "the genetic changes that occur are remarkably few." Prominent among these changes were



Deep sequencing has revealed more evidence that, in diseases such as acute myeloid leukemia, chemotherapy may lead to new mutations that may drive resistance. *Wikimedia Commons/Paulo Henrique Orlandi Mourao*

transversions, substitutions of a purine for a pyrimidine or vice versa, that are associated with DNA damage. The frequency of transversions was 46% for relapse-specific mutations but only 31% for primary tumor mutations.

DiPersio emphasizes that the study does not show chemotherapy actually causes the mutations; that remains to be proven. He also says it will be important to compare these results to relapse from other kinds of therapy. A more daunting task is to determine why some founding clones persist, and which mutations actually contribute to relapse. It may be possible, he adds, to identify genetic markers that predict whether certain cancers will persist.

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AACR American Association for Cancer Research

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