Team shows cancer chemotherapy accelerates 'molecular aging'

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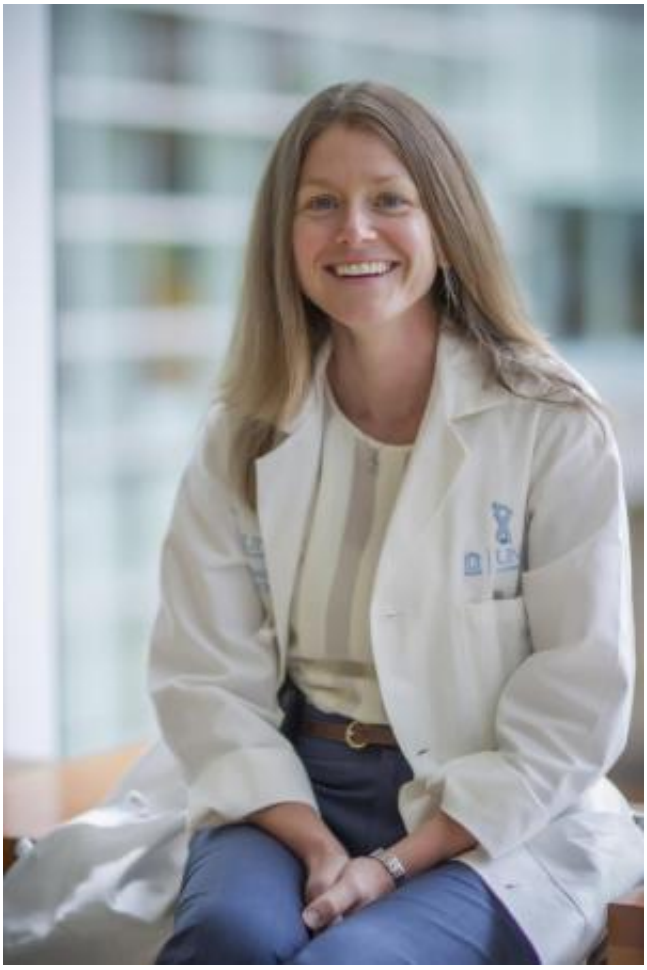

The study, headed by Hanna Sanoff, M.D., M.P.H., assistant professor with the UNC School of Medicine and member of UNC Lineberger, is published in this week's *Journal of the National Cancer Institute*. Credit: UNC Lineberger Comprehensive Cancer Center

Physicians have long suspected that chemotherapy can accelerate the aging process in patients treated for cancer. Using a test developed at UNC Lineberger Comprehensive Cancer Center to determine molecular aging, UNC oncologists have directly measured the impact of anti-cancer chemotherapy drugs on biological aging.

Researchers measured the level of p16, a protein that causes cellular aging, in the blood of 33 women over the age of 50 who had undergone chemotherapy for curable breast cancer. Samples were taken for analysis of molecular age from patients before chemotherapy, immediately following chemotherapy and a year after therapy finished. The analysis showed that curative chemotherapy also caused an increase in a patient's molecular age that on average was equivalent to 15 years of normal aging. The same was true in a separate group of 176 breast cancer survivors who had received chemotherapy on average three and a half years prior.

The study, headed by Hanna Sanoff, MD, MPH, assistant professor with the UNC School of Medicine and member of UNC Lineberger, is published in this week's *Journal of the National Cancer Institute*. Dr. Sanoff said that the results indicate that the p16 test holds promise as a means of evaluating how chemotherapy will affect a patient's long-term health and survival and as a predictive biomarker for the long-term toxicity of chemotherapy.

"Our theory is that if you have an advanced molecular age to begin with, it will be harder for you to tolerate chemotherapy," said Dr. Sanoff. "We believe a high level of p16 before treatment could mean that a patient will have a harder time making new blood cells after each chemotherapy treatment, and therefore be at greater risk for anemia and infection during chemotherapy."

The key role of p16 in human aging has been established over the last

decade in the lab of UNC Lineberger Director Dr. Norman Sharpless. Research conducted in Sharpless' lab showed in 2004 that the levels of p16 increase exponentially with aging, and developed the p16 blood test for human use in 2009.

The next direction for this research, ongoing under the leadership of Dr. Hyman Muss, director of UNC Lineberger's Geriatric Oncology Program, involves determining if markers of molecular age predict patients' physical function and outcome in a number of clinical settings.

"While these findings are highly provocative, we have much more to study and will have to verify in future trials how these changes in molecular aging affect long term survival," said Dr. Muss. "Adjuvant chemotherapy has dramatically improved breast cancer survival and pending further data, the results of our study should not effect adjuvant chemotherapy decisions."

The p16 test seems particularly well-suited as an aging marker for this purpose as it plays a causal role in biological aging, is strongly correlated with chronological aging, and increases exponentially in response to pro-aging stimuli. Dr. Sanoff said she believes the test has promise as the basis of a clinical tool allowing physicians to evaluate the degree to which a given treatment accelerates biological and physical aging.

Provided by University of North Carolina Health Care

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