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Adjuvant chemotherapy increases markers of molecular aging in the blood of BC survivors

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Adjuvant chemotherapy for breast cancer is "gerontogenic", accelerating the pace of physiologic aging, according to a new study published March 28 in the *Journal of the National Cancer Institute*.

Loss of organ function, characterized by an increase in cellular senescence, is one physiological part of aging. Studies have identified leukocyte telomere length, expression of senescence-associated cytokines including interleukin-6, and expression of p16INK4aand ARF in peripheral blood T lymphocytes (PBTLs) as markers of cellular senescence. The authors previously showed p16INK4a is a marker of accelerated molecular age in PBTLs associated with smoking, physical inactivity, and chronic human immunodeficiency virus infection. To date, the long term effect of cytotoxic chemotherapy given with curative intent on molecular aging has not been reported.

Hanna K. Sanoff, M.D., Norman E. Sharpless, M.D., and Hyman B. Muss, M.D., and their colleagues prospectively collected blood and clinical data from 33 women with stage I-III breast cancer before, immediately after, 3 months after, and 12 months after anthracycline-based chemotherapy. Blood was analyzed for markers of cellular senescence. They observed increased expression of the senescence markers p16INK4a and ARF in PBLTs immediately after chemotherapy, and which remained elevated for at least a year after treatment. In an independent cohort of 176 breast cancer survivors, prior chemotherapy was associated with a persistent increase in p16INK4a at an average of 3.4y after treatment. These results suggest the age-

promoting effects of chemotherapy last for several years after treatment, and may be permanent.

The authors conclude, "We have shown that cytotoxic chemotherapy potently induces the expression of markers of cellular senescence in the hematologic compartment in vivo, comparable with the effects of 10 to 15 years of chronologic aging in independent cohorts of healthy donors." Further studies are underway.

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