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CHEMOTHERAPY

Life gained, years lost?

New data demonstrate that chemotherapy causes a rapid increase in molecular markers of cellular senescence. Although mostly indicative of ageing of the haematopoietic system, these results indicate that molecular ageing might explain some of the delayed adverse events linked to cancer therapy.

The new data show that, in particular, levels of $p16^{INK4}$ mRNA, a key marker of senescence, increased by 75% in peripheral T cells from 33 patients with breast cancer after adjuvant chemotherapy. According to previously reported rates of change in $p16^{INK4}$ expression with ageing "the increase in molecular age caused by chemotherapy was on average the same as 10–15 years of chronological ageing," says Norman Sharpless, one of the leaders of the study.

"It seems this increase in molecular age persists for several years (if not forever)," continues Sharpless. In a retrospective cohort of 176 patients treated up to 18.8 years prior to analysis, chemotherapy increased molecular age by the equivalent of 10.4 years of chronological ageing compared with patients not exposed to chemotherapy.

Although most patients showed some increase in molecular ageing after chemotherapy, the effect size was highly variable. Thus, "a patient's molecular age might predict toxicity from a planned therapy," claims Sharpless "as patients who are physiologically older might exhibit more severe toxicity or disease than those who are physiologically younger, but have the same chronological age."

Quantification of molecular ageing could also be important to discern the long-term effects of various chemotherapy regimens, thus potentially leading to improved treatment approaches. "It is very important to note, however, that chemotherapy can cure breast cancer, and the cost of increased molecular ageing is likely worth the benefit of an increased rate of cancer cure," Sharpless concludes.

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Original article Sanoff, H. K. *et al*. Effect of cytotoxic chemotherapy on markers of molecular age in patients with breast cancer. *J. Natl Cancer Inst*. doi:10.1093/jnci/dju057