Tipping the balance between senescence and proliferation

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An arrest in cell proliferation, also referred to as cellular senescence, occurs as a natural result of aging and in response to cellular stress. Senescent cells accumulate with age and are associated with many aging phenotypes, and removal of these cells by the immune system is important for preventing cancer and other disorders. The tumor suppressor p53 coordinates a signaling network that is important for cell arrest. p53 is produced as various isoforms as the result of alternative splicing and promoter usage. One isoform, p53β, accelerates cellular arrest, while another isoform, Δ133p53 represses replicative senescence in cultured cells.

In this issue of the *Journal of Clinical Investigation*, Abdul Mondal and colleagues at the National Cancer Institute evaluated the expression of these two p53 isoforms in T lymphocytes from healthy donors and donors with lung cancer. In healthy patients, the authors observed an age dependent accumulation of senescent cells and that these cells had an increase in p53β compared to Δ133p53. In lung tumor-associated cells, there was a higher level of the Δ133p53 isoform. Furthermore, in senescent cells, expression of Δ133p53 induced replication and proliferation, while induction of p53β in tumor-associated cells promoted senescence.

This study defines the contribution of two p53 isoforms to senescence regulation, and suggests that altering the Δ133p53:p53β ratio may be an effect therapeutic strategy for treating immunosenescence disorders.

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