

# Abstract

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## Roles of tumor suppressor and telomere maintenance genes in cancer and aging--an epidemiological study.

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**OBJECTIVE AND METHODS:** Advanced age is strikingly linked to increased incidence of cancer. To gain insight into the mechanism underlying the association between increased cancer incidence and aging in normal human physiological conditions, we used a case-control design and measured the mRNA expression levels of p53, ATM, hTERT and TRF2, the four major protectors of genomic integrity, in isolated peripheral blood lymphocytes from 202 confirmed bladder cancer (BC) patients and 199 healthy controls.

**RESULTS:** Significant age effects on expression levels were observed. When we divided the study subjects into three age groups (<57, 57-65 and > or = 65), the expressions of p53, ATM and TRF2 significantly decreased with advancing age in cases (P for trend < or = 0.001, 0.01 and 0.01 for p53, ATM and TRF2, respectively). In controls, however, p53 expression significantly increased with advancing age (P for trend = 0.05). Among subjects > or = 65 years of age, the expressions of p53, ATM and TRF2 were significantly lower in cases than in controls (P = 0.003, 0.04 and 0.05 for p53, ATM and TRF2, respectively), suggesting that attenuated genomic maintenance mechanisms lead to increased cancer risk in older individuals. When we dichotomized our study population at the median age of study subjects (61 years old), low p53 expression was associated with a significantly increased BC risk in older people (OR = 2.27, 95% CI = 1.00-5.16). In addition, older subjects without detectable hTERT expression had a significantly reduced BC risk (OR = 0.41, 95% CI = 0.17-0.99).

**CONCLUSIONS:** Our study provides the first epidemiologic evidence that the increased genomic instability resulting from the combination of telomere dysfunction, impaired ATM- and p53-mediated DNA damage, and/or telomere dysfunction response pathway contributes to increased cancer incidence in the elderly population.

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