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Titel des Beitrags:
Inhibition of telomerase induces alternative lengthening of telomeres during human esophageal carcinogenesis.

Abstract:
Immortalization is an important step toward the malignant transformation of human cells and is critically dependent upon telomere maintenance. Two mechanisms are known to maintain human telomeres. The process of telomere maintenance is either mediated through activation of the enzyme telomerase or through an alternative mechanism of telomere lengthening called alternative lengthening of telomeres (ALT). Whereas 85% of all human tumors show reactivation of telomerase, the remaining 15% are able to maintain telomeres via ALT. Telomerase inhibitors are already investigated in clinical trials, although the regulation as well as potential coexistence and redundancy of both telomere maintenance mechanisms during distinct steps of carcinogenesis are poorly understood. Herein, we demonstrate that telomerase activity and ALT alternate in a cell cycle dependent fashion in human esophageal epithelial cells, and can coexist in a genetically defined model of oral-esophageal squamous carcinogenesis. Moreover, we show that immortalized premalignant cells as well as cancer cells are able to switch from telomerase activation to ALT upon inhibition of telomerase. This indicates that cancer cells treated with telomerase inhibitors can use alternative and adaptive ways to maintain their telomeres and thereby escape telomere-based therapeutic