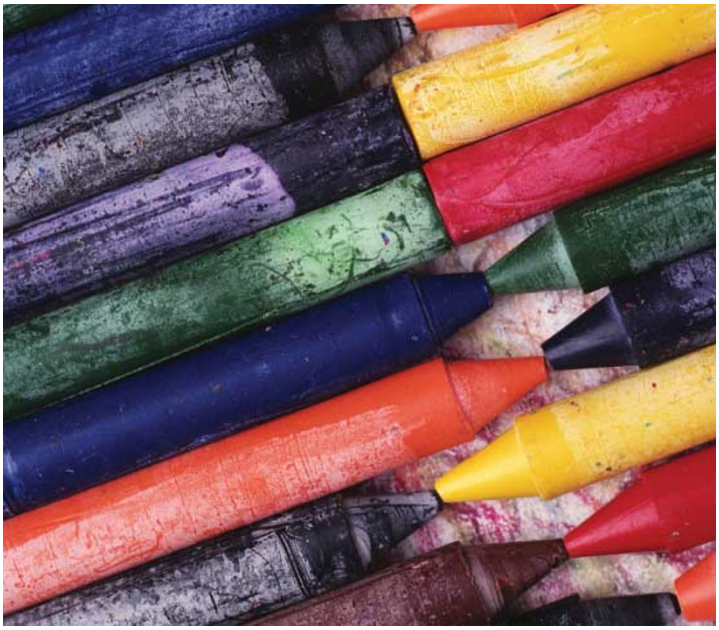
HIGHLIGHTS

TELOMERES

The long and the short of it



Is telomere-length control a matter of elongation efficiency, with the telomerase enzyme being recruited to all telomeres but having increased activity on shorter telomeres? Or does telomerase act on a subset of telomeres, its recruitment being dependent on telomere length? In *Cell*, Joachim Lingner and colleagues now provide evidence for the latter model.

To study the mechanisms of telomere-length homeostasis, Lingner and colleagues developed a system for measuring single telomere-elongation events *in vivo*. They used a *Saccharomyces cerevisiae* strain that was deficient for telomerase and reintroduced the enzyme by mating with a wild-type strain. Telomeres from the original telomerase-negative strain were then amplified by PCR, cloned and sequenced. Yeast telomerase produces irregular telomeric DNA sequences, which was sufficient to distinguish individual telomere-elongation events from each other.

By measuring telomere elongation over the course of a single cell cycle, the authors showed that within one cell cycle, less than 40% of telomeres were extended. This implies that telomere-length homeostasis is not regulated by the enzymatic activity of telomerase, as suggested by the first model.

When Lingner and co-workers compared the extent of telomere elongation with telomere length, they found that telomere extension length was highly variable and independent of their original telomere length. But, when they sorted telomeres according to their length and plotted the average telomere length against the frequency of elongation, the correlation was significant. In fact, the shortest telomeres were 6 times more likely to be elongated than the longer, wild-type-length telomeres.

So, how does telomere length regulate the frequency of telomere elongation? It has been known for some time that certain telomere-binding proteins, such as Rap1 in *S. cerevisiae*, are involved in a negative-feedback mechanism that regulates telomere length. This so-called 'protein-counting mechanism' transmits information about the length of the telomere on the basis of the number of telomere-bound proteins. The Rif1 and Rif2 proteins, which are recruited to telomeres by Rap1, are thought to mediate the Rap1-counting mechanism of telomere-length control.

The authors found that, in the absence of either Rif1 or Rif2, the frequency of telomere elongation was about twofold higher compared with wild-type strains. So, they suggested that Rif1 and Rif2 promote the nonextendible telomeric state in which telomere elongation is somehow blocked.

Based on their findings, Lingner and colleagues propose a binary-switch model in which long telomeres recruit a lot of the Rap1–Rif1–Rif2 complex, which causes the telomeres to switch to a nonextendible state. But, when telomeres get shorter and lose most of the complex, they become extendible. It is this equilibrium between the two telomere states that maintains telomere length.

Arianne Heinrichs

References and links

ORIGINAL RESEARCH PAPER Teixeira, M. T. *et al.* Telomere length homeostasis is achieved via a switch between telomerase-extendible and -nonextendible states. *Cell* **117**, 323–335 (2004)