



TELOMERES

Splicing uncoupled



...a direct role for the spliceosome in the maturation of TER1.



The telomerase enzyme complex controls telomere length, and uses telomerase RNA as a template to add telomeric repeats to chromosome ends by reverse transcription. In fission yeast, the *ter1*⁺ gene encodes telomerase RNA (or TER1). Box *et al.* now reveal how mature TER1 is derived from longer transcripts.

The authors noticed that the longer precursor transcripts contain an intron with putative splice sites and a branch point sequence. Mutation of the splice sites and the branch point resulted in impaired splicing. Mutations in the 5' splice site and the branch point caused a marked reduction in the mature form of TER1 and telomere shortening. A splicing defect owing to a mutation in the 5' splice site was rescued by co-expressing mutant U1 spliceosomal RNA that contained the compensatory nucleotide change, and resulted in sufficient amounts of functional TER1 to maintain telomere length. Together, these findings suggest a direct role for the spliceosome in the maturation of TER1.

By contrast, mutating the 3' splice site did not affect the formation of mature TER1 nor telomere length.

Moreover, the 3' end of mature TER1 maps precisely upstream of the 5' splice site, which suggests that TER1 maturation might involve only the first step (cleaving the 5' end of the intron) but not the second step of a standard splicing reaction (cleaving the 3' end of the intron). This also means that the spliceosome must be prevented from completing the second reaction, as this would result in a different 3' end for mature TER1. An unusually long distance between the branch point and the 3' end of the intron prevents efficient completion of the second splicing step; indeed, reducing the distance led to the accumulation of the fully spliced form and a reduction in mature TER1.

It will be interesting to investigate whether the functional uncoupling of the first and second step of splicing by the spliceosome represents a more general mechanism for RNA 3'-end formation, and whether this mechanism for telomerase RNA maturation applies to species other than fission yeast.

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ORIGINAL RESEARCH PAPER Box, J. A. *et al.* Spliceosomal cleavage generates the 3' end of telomerase RNA. *Nature* **456**, 910–914 (2008)