

Abstract

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Telomeres and the DNA damage response: why the fox is guarding the henhouse.

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BACKGROUND: DNA double strand breaks (DSBs) are repaired by an extensive network of proteins that recognize damaged DNA and catalyze its repair. By virtue of their similarity, the normal ends of linear chromosomes and internal DNA DSBs are both potential substrates for DSB repair enzymes. Thus, telomeres, specialized nucleo-protein complexes that cap chromosomal ends, serve a critical function to differentiate themselves from internal DNA strand breaks, and as a result prevent genomic instability that can result from their inappropriate involvement in repair reactions.

DISCUSSION: Telomeres that become critically short due to failure of telomere maintenance mechanisms, or which become dysfunctional by loss of telomere binding proteins, elicit extensive checkpoint responses that in normal cells blocks proliferation. In this situation, the DNA DSB repair machinery plays a major role in responding to these "damaged" telomeres - creating chromosome fusions or capturing telomeres from other chromosomes in an effort to rid the cell of the perceived damage. However, a surprising aspect of telomere maintenance is that many of the same proteins that facilitate this repair of damaged telomeres are also necessary for their proper integrity.

SUMMARY: Here, we review recent work defining the roles for DSB repair machinery in telomere maintenance and in response to telomere dysfunction.

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