Preface

Pioneering experiments of Hermann Joseph Muller and Barbara McClintock carried out in the 1930's suggested that chromosome ends or telomeres have protective properties essential for chromosome segregation. Although Muller and McClintock relied exclusively on cytological methods that lacked the power of insight routinely available in most laboratories today, modern methods fully support their prediction that telomeres are essential protective 'caps'. We know today that, in most organisms, telomeres are composed of evolutionarily conserved repetitive DNA sequences bound by a set of proteins that facilitate formation of a loop structure. The loops, known as T-loops, presumably act as protective 'caps' essential for keeping chromosomes as individual entities.

Another interesting prediction was associated with the field of telomere biology. A Russian theoretical biologist, Alexey Olovnikov, predicted, about 40 years ago, that conventional DNA replication enzymes would not be able to completely replicate DNA at chromosome ends and formulated the 'end replication problem'. He also predicted the existence of telomerase, an enzyme that synthesizes telomeric DNA. Olovnikov's predictions attracted the interest of gerontologists and cancer biologists. Telomerase is strongly associated with the process of cell immortalization, a key step in development of cancer. Many scientists think that inhibition of telomerase in cancer cells can limit their proliferative capacity and thus stop tumor growth.

Looking back at the history of telomere biology, one curiosity is evident. For example, Muller performed his pioneering experiments on *Drosophila melanogaster*. From a perspective of today's telomere molecular biologist, *Drosophila* is a highly unusual organism. In contrast to a large majority of organisms in which telomeres are composed of a conserved repetitive DNA sequence and a set of proteins that enable formation of T-loops, *Drosophila* shows a dramatic difference. *Drosophila* telomeres are composed of retrotransposons and there is no evidence that T-loops exist at *Drosophila* telomeres. Yet, using *Drosophila* as a model, Muller was able to correctly predict a protective function of telomeres universal to all eukaryotes. This suggests that there is more than one type of telomere structure that provides its function. The question then arises as to whether there is any common feature that different types of telomere structure (i.e., *Drosophila* and canonical) must share in order to perform essential function. A series of recent observations in different organisms suggest that this common feature may be an inter-dependence between telomere maintenance and DNA damage response mechanisms which is becoming increasingly apparent. For example, irrespective of the type of telomere structure, failure of essential DNA damage response molecules including DNA damage signaling kinase ATM (ataxia telangiectasia mutated) or a protein complex MRN (MRE11, RAD50, NBS) involved in DNA damage sensing and some other proteins will affect telomere function in both *Drosophila* and organisms with canonical telomeres (see cover illustration). The message here is that telomere function may be inextricably linked with DNA damage response mechanisms and that this link is essential for telomere function.

The current themed issue is an attempt to present recent developments in the multifaceted field of telomere biology and its impact on understanding not only chromosome structure and evolution but also applied fields such as carcinogenesis and ageing. I would like to thank all contributors for their excellent efforts and referees for their expert work. I am also grateful to Michael Schmid, Chief Editor of the journal, for giving me the opportunity to edit this themed issue.

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