
Book Reviews

The Telomere. By DAVID KIPLING. Oxford University Press. 1995. 208 pages. Price Hardback £45 ISBN 0 19 963467 X, Paperback £22.50 ISBN 0 19 963600 1.

This is an excellent little book on a phenomenon first discovered by Herman Muller in the 1930s, which remained full of mystery under intensive study by cytogeneticists for the next 40 years or so, and was not entirely solved when the molecular geneticists got busy on it in the late 70s. Current research should clear up the main problems in the next few years, and this increasingly rapid progress makes Kipling's book a very timely introduction to the telomere mystery. The term 'telomere' was invented by Muller for the natural ends of eukaryotic chromosomes, which appeared to act as seals, essential for the chromosome's survival, since his very extensive study of X-ray-induced chromosome breaks in *Drosophila* failed to produce any deletions or inversions involving a chromosome end. Kipling's book takes us through the successive stages of research on telomeres, the mysteries solved and the further mysteries revealed.

His ten chapters include (1) an introduction describing the end-replication problem due to the fact that lagging strand synthesis leaves a small gap at the end of the molecule, and if this missing end is not replaced the chromosome will be shortened at every cell division. A special enzymatic activity (telomerase) which adds telomeric sequence to the longer strand so that lagging strand synthesis can lengthen the other strand and maintain chromosome length, has been identified in a few species and may be present in most. Chapter 2 discusses the many studies of the cytology of the telomere, which suggest several possible functions for the telomeres. The telomere structure (chapter 3) consists of (or at least includes) tandem repeat arrays of a short sequence at the very end of the chromosome, with considerable similarity in sequence between different species. In any cell all chromosome ends have the same nucleotide sequence. Among the 24 species listed, six including humans, mouse and several fungi, have the identical repeated sequence TTAGGG, and only *Candida albicans* and *Drosophila melanogaster* differ strikingly. Subterminal sequences may also play a part in telomere function.

Telomerase activity (chapter 4) has only been

identified so far in three ciliate species, *Tetrahymena*, *Oxytricha* and *Euplotes*, and in humans and mice, probably because few other species have been investigated biochemically, but Kipling concludes that 'a telomerase model can rationalize, or at least be consistent with, many of the observed structural features of telomeres'. Chapter 5 discusses telomere proteins: 'the best characterized yeast telomere binding protein, RAP1, has additional well-defined roles as a transcriptional regulator at non-telomeric loci. The precedent of its multiple functions illustrates the caution required before dismissing any unexpected telomere binding activity as irrelevant'. Chapter 6 discusses genome rearrangements and telomeres, and chapter 7 takes up the still controversial questions of human telomere loss, ageing and cancer. Human telomeres shorten with age *in vivo* so that telomere length is an excellent biomarker for the potential number of cell divisions remaining. Certain human syndromes lead to premature ageing, which is correlated with reduced length of their telomeres, but it remains unknown whether the shorter telomeres reflect a higher rate of sequences loss or simply a greater rate of cell turnover. Shortened telomeres are also found in some human tumours, but this could be due to the increased number of cell divisions in the tumour cells compared to normal tissue, so the question of whether cancer can be caused by telomere loss seems still open. Another intriguing question is why telomere activity seems to be absent in somatic cells.

The remaining chapters discuss 'Chromatin structure and position effects', 'The structure and maintenance of *Drosophila* telomeres' (which is dramatically different from the other species analysed), and finally, in chapter 10, 'Telomeres and mammalian genome analysis'. Each chapter has an extensive and up-to-date bibliography, divided into reviews and primary papers (a reference that caught my eye because of its intriguing title was A. W. Murray (1993) Sunburnt fission yeast, *Nature* 363, 302). Thoroughly recommended and cheap at the price in paperback.

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