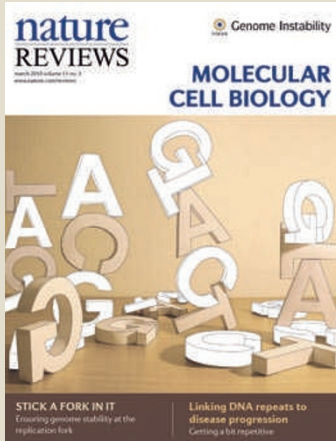




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► **COVER:** 'Genome Instability' by Vicky Summersby, inspired by the Focus starting on p165



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The integrity of the genome is crucial for tumour suppression and the propagation of genomic information. DNA damage can result from cellular metabolism, routine errors in DNA replication and recombination, and exogenous genotoxic agents. To combat these attacks, cells have evolved a response system that induces cell cycle arrest, allowing sufficient time for DNA repair by specialized proteins. The DNA damage response system activates the appropriate DNA repair pathway or, in the case of irreparable damage, induces apoptosis.

Recent advances have increased our understanding of the DNA damage response and the origin of genomic rearrangements in both mice and humans. This special Focus on Genome Instability (www.nature.com/nrm/focus/genome-instability) highlights some of the key mechanisms devised to maintain genome integrity and discusses the potential outcomes of genome instability. The Review on page 171 focuses on how telomeres protect the ends of chromosomes and prevent genome instability. Two Reviews on homologous recombination discuss genome stability and instability in the germ line (page 182) and in somatic cells (page 196). Another Review describes mechanisms that help to maintain genome stability at the replication fork (page 208). The consequences of chromosomal instability for tumorigenesis and cancer progression are discussed on page 220. Finally, a Progress article (page 165) provides the latest insights into the mechanistic basis of trinucleotide repeat instability.

Accompanying this issue is a Poster by Eric J. Bennett, Mathew E. Sowa and J. Wade Harper, which illustrates the different deubiquitinating enzyme (DUB) families and highlights the cellular pathways in which some DUB-associated complexes act. The Poster (www.nature.com/nrm/posters/dubs) was produced with generous support from Boston Biochem.

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