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► **COVER:** 'Actin tree' by Vicky Askew, inspired by the Review on p713



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The efficient replication of DNA is due in part to the high processivity of chromosomal replicases, a quality endowed by sliding-clamp proteins that secure the DNA polymerase to the DNA template. At the replication fork, sliding clamps are loaded onto DNA by the clamp-loader complex, which is composed of multiple ATPase subunits. Although clamp loaders from different organisms differ in the way they use ATP, their structure and mechanisms of action show striking similarities across the three domains of life, as discussed on page 751 by Chiara Indiani and Mike O'Donnell.

The Review by Patrick Sung and Hannah Klein (page 739) features another highly conserved cellular apparatus — the protein machinery involved in homologous recombination (HR). HR generates genome diversity by facilitating genetic exchange at meiosis and at the same time preserves genome fidelity through its crucial role in DNA repair. Sung and Klein detail the intricacies of the HR reaction, outlining the mechanistic principles of the recombinase enzymes that form the catalytic core of the HR machinery. Various regulatory factors, including the tumour suppressor BRCA2, have recently been shown to modulate HR efficiency, implicating the impairment of HR in the development of breast, ovarian and other cancers.

Although mutations in the structural muscle protein dystrophin have long been known to cause muscular dystrophies, there is a growing realization that defects in non-structural skeletal-muscle components, such as enzymes and signalling molecules, can also cause muscular dystrophies. On page 762, Kay E. Davies and Kristen J. Nowak review the array of defective proteins that cause these crippling disorders. On a positive note, they highlight promising therapeutic approaches that might translate our increased knowledge of the dystrophic process into long-awaited clinical treatments.

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