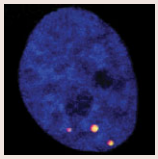
In this issue



Long telomeres without telomerase

Many tumour cells avoid senescence by activating telomerase, which prevents telomere shortening and facilitates unlimited proliferation. However, 10–15% of cancer cells maintain telomere length differently: the alternative lengthening of telomeres (ALT) pathway involves both DNA repair and recombination. ALT-associated promyelocytic leukaemia (PML) nuclear bodies (APBs) – unique nuclear structures that contain telomeres and proteins associated with them – are specifically found in cells that undergo ALT and colocalise with proteins involved in DNA repair and recombination. However, a direct link between APBs and telomere lengthening has not yet been shown. On page 3603, Karsten Rippe and colleagues now elucidate the steps involved in APB biogenesis and the induction of ALT. They show that enrichment at telomeres of the nuclear body components PML and Sp100, the SUMO E3 ligase MMS21 as well as SUMO1 itself, the recombination factor NBS1 or the shelterin subunits TRF1 and TRF2 can nucleate APB formation. Other proteins, such as the recombination factors Rad9, Rad17 and Rad51 are, however, secondarily recruited to the APB. Furthermore, the de novo assembly of APBs induces double-strand break repair and leads to telomere repeat extension, which suggests that ALT is regulated by a multi-step process of initiation, complex assembly, DNA repair and, finally, telomere elongation.