

S015 Chromosomal instability in the pathogenesis and treatment of cancer

Ashok R. Venkitaraman

University of Cambridge, UK

Instability of chromosome structure or number is a hallmark of common epithelial malignancies. Accurate prosecution of the cellular response to double-strand DNA breaks (DSBs) is essential for the suppression of chromosomal structural anomalies in dividing cells. Phosphorylation by PIK kinases of the variant histone, H2AX, which recruits the machinery for DSB repair, is the earliest known marker of DNA breakage. A new signalling pathway, proximal to H2AX modification, which promotes chromatin changes that trigger the DNA damage response will be reported (1).

Germline mutations in the breast cancer susceptibility gene, BRCA2 give rise to numerical and structural chromosomal aberrations (reviewed in 2,3). One major function of BRCA2 is in the control of the RAD51 recombinase during the reactions that lead to DSB repair by homologous DNA recombination. Recent results, in which Varshavsky's N-end rule has been used to create a thermosensitive form of RAD51 in vertebrate cells, enabling dissection of the cell cycle co-ordination of DNA replication with homologous recombination, will be reported (4).

References

1. Ayoub N.A., A.D. Devaprasath, J.A. Bernal & A.R. Venkitaraman (2008). Nature 453: 682-6.
2. Venkitaraman, A. R. Cell 108, 171-82 (2002).
3. Venkitaraman AR. 2008. Annu Rev Pathol
4. Su, X., J.A. Bernal & A.R. Venkitaraman (2008). Nature Struct Mol Biol [Advance Online Publication doi 10.1038/nsmb.1490]