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TUMOUR SUPPRESSION BY BRCA2: A CONNECTION WITH DNA REPLICATION

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Inherited mutations affecting the BRCA2 tumour suppressor predispose to breast, ovarian and other cancers. BRCA2-deficient cells exhibit instability of chromosome number and structure, and spontaneously accumulate aberrant chromosomes during cell division (1). Evidence will be presented that the spontaneous chromosomal instability that follows BRCA2 inactivation arises from an essential function for BRCA2 in the response to stalled DNA replication (2). Using two-dimensional gel electrophoresis, we have examined the structure of DNA replication intermediates in BRCA2-deficient cells. After genome-wide replication stalling, Y-shaped DNA junctions at stalled replication forks collapse in cells that lack BRCA2, accompanied by the appearance of double-strand DNA breaks. The implications of our findings for understanding BRCA2's biological functions and its role in tumour suppression will be discussed.

References.

1. Venkitaraman, AR (2002) Cell 108, 171
2. Lomonosov, M et al (2003) Genes Dev 17, 3019