

S006 Genomic instability and cancer: lessons from analysis of Bloom's syndrome

Ian D. Hickson

Weatherall Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital, Oxford, OX3 9DS, UK

Bloom's syndrome (BS) is an autosomal recessive disorder associated with short stature, sunlight sensitivity, and a greatly elevated level of cancers of all types. The BS gene product, BLM, is a RecQ family DNA helicase that can also promote branch migration of Holliday junctions. BLM forms an evolutionarily-conserved complex with topoisomerase III and a twin OB-fold containing factor called RMI1. Previously, we reported that this protein complex, which we will refer to as the BTR complex, could catalyze a process called Holliday junction dissolution whereby interlinked DNA molecules containing a double Holliday junction are processed exclusively into non-cross-over products. This reaction is proposed to allow the faithful completion of homologous recombination events without associated genomic instability. A fourth member of the BTR complex, which also contains an OB-fold, was identified recently in Weidong Wang's group and is termed RMI2. This factor does not appear to influence dissolution, but is important *in vivo* for stability of the BTR complex. Our recent evidence indicates that the BTR complex can also catalyze the unlinking of two DNA molecules that mimic a late-stage replication intermediate where two replication forks converge. In a search for downstream consequences of a failure to effect decatenation of replication and/or recombination intermediates, we identified ultra-fine anaphase bridges that had escaped detection previously because they do not contain histones or stain with commonly used DNA dyes. Our recent data indicate that these bridges are derived from specific chromosomal loci. A potential mechanism by which the BTR complex suppresses the accumulation of anaphase bridges will be discussed.