

P019 The C-terminus of Brca2 links the disassembly of Rad51 complexes to the timing of mitotic entry

Nabieh Ayoub, Eeson Rajendra, Xinyi Su, Anand D. Jeyasekharan, Robert Mahen and Ashok R. Venkitaraman

The Medical Research Council Cancer Cell Unit, Hutchison/ MRC Research Centre, Hills Road, Cambridge CB2 2XZ, United Kingdom.

The tumour suppressor Brca2 controls the Rad51 recombinase during homologous DNA recombination (HR), via the evolutionarily conserved BRC repeats, and a distinct, carboxyl (C)-terminal motif whose Rad51-binding ability is regulated by cyclin-dependent kinase (CDK) phosphorylation. Here, we report an unrecognized function for the C-terminal motif of Brca2 in coordinating HR with mitosis. We show that the avian C-terminal motif is functionally cognate with its human counterpart, and identify point mutations that either abolish or enhance Rad51 binding. Using ‘hit-and-run’ gene targeting to insert single-codon substitutions into the avian *Brca2* locus, we unexpectedly find that these mutations affect neither the formation of damage-induced nuclear foci containing Rad51, nor DNA repair by HR. Instead, foci disappear more rapidly in a point mutant that fails to bind Rad51, associated with faster mitotic entry. Conversely, the slower dissipation of foci in a point mutant that constitutively binds Rad51 correlates with delayed mitosis. Thus, Rad51 binding by the C-terminal Brca2 motif is dispensable for HR: instead, it links the disassembly of Rad51 complexes to mitotic entry. This mechanism may ensure that HR terminates before chromosome segregation.