

S012 The role of BRCA1 in the repair of DNA damage

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Inheritance of a mutation in *BRCA1* results in predisposition to early onset breast and ovarian cancer. Tumours in these individuals arise after somatic mutation or loss of the wild type allele. Loss of BRCA1 function leads to a profound increase in genomic instability involving the accumulation of mutations, DNA breaks and gross chromosomal rearrangements. Accordingly BRCA1 has been implicated as an important factor involved in both the repair of DNA lesions and in the regulation of cell cycle checkpoints in response to DNA damage.

Here I will report on two projects to understand the molecular function of BRCA1 and show how physical interactions made between BRCA1 and several different partner proteins facilitate its role in DNA repair. Firstly, I will discuss how BRCA1 preserves genetic integrity through its role in a molecular switch that shifts the balance of repair of double strand breaks from a potentially mutagenic end-joining pathway to more accurate homologous recombination during the cell cycle. Secondly, I will highlight a role for BRCA1 in the maintenance of potentially unstable G4 DNA signatures in the genome and suggest how this might be exploited for therapy.