Tumor suppressor C53 interacts with BRCA2, regulates DSB repair and drives breast and ovarian cancer prognosis

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BRCA2 is an essential protein for DNA repair by homologous recombination and its deficiency leads to genome instability and tumor progression. By means of a yeast two-hybrid screen, we identified NF-κB-dependent tumor suppressor C53 as a new BRCA2 helical domain interacting protein. C53 inhibition leads to resistance to a variety of DNA damage agents and increased spontaneous and ionizing radiation-induced chromosome fragility. Resembling BRCA2, C53 is required for homologous recombination and its absence markedly upregulates single strand annealing. Finally, we show that low C53 expression strongly correlates with poor patient survival rates in over 3.500 breast and 300 ovarian cancer datasets. Our results therefore uncover a new player in DNA repair by homologous recombination and single strand annealing that modulates the prognosis of breast and ovarian cancer patients.