Characterization of Brca1 Degradation/Stability Regulatory Elements

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Alterations of BRCA1 gene are the major determinants in genetic susceptibility of hereditary breast cancer, and also play an important role in ovarian cancer development. BRCA1 is involved in DNA damage repair pathway, it has been suggested that it functions as a scaffold or platform to coordinate different activities needed for repair. The correct expression of BRCA1 protein is essential for its work in cellular processes. The physiological levels of this protein vary in cell cycle progression, although the molecular mechanisms and motifs underlying this process were not fully elucidated. In this study we investigate the role of BRCA1 exon 14 region in the control of protein degradation/stability. Using ectopically transfected mammalian expression plasmids containing BRCA1 wild type region comprising the exon 13 to exon 24 (WT, aa 1396-1863), or a similar construct lacking the exon 14 region (delta14 aa 1456-1494) in HEK293T cells, we demonstrated that the degradation of the resulting protein were extensively impaired in the delta14 transfected cells treated with a protein synthesis inhibitor. These observations were confirmed in a flow cytometry approach using BRCA1 WT or delta14 fusioned with green fluorescent protein. In this model the protein degradation were decreased in about 2.5 times when compared to the WT protein. Collectively these data suggest that BRCA1 exon 14 region comprises one or more putative regulatory elements of protein degradation. Keywords: BRCA1, breast cancer, protein degradation.