P48 Downregulation of BRCA1 and CTCF in clear cell renal cell carcinoma

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Introduction & Objectives: BRCA1 and CTCF both are involved in DNA double strand break repair pathway by homologous recombination (HR). BRCA1 is commonly mutated in triple negative breast cancer (TNBC), which characterized by FBP1 loss and metabolic switch. FBP1 loss was also observed in clear cell renal cell carcinoma (ccRCC) and metabolic aberrations are common in this type of cancer. Here, we evaluated the level of BRCA1 and CTCF proteins level in ccRCC patient samples and anti-cancer effect of olaparib in treating renal cancer.

Materials & Methods: Immunohistochemistry staining of BRCA1 and CTCF was used to determine the proteins level in cancer cells compare to normal kidney tissue. Clonogenic assay, MTT test and growth study was performed to study the sensitivity of kidney cancer cell lines for olaparib. Next generation sequencing (NGS) was used to identified mutations in BRCA1 and BRCA2 genes. qRT-PCR and microarray reanalysis was performed to determine the transcript level of BRCA1 and CTCF follow by survival rate.

Results: Both BRCA1 and CTCF was significantly decreased in ccRCC samples compare to normal kidney tissue. This decreasing was independent on gender and Fuhrman grade. The deep NGS analysis revealed no mutation in BRCA1/2 genes except one single somatic missense mutation in BRCA1 gene in one patients. Moreover, the BRCA1 transcript level was significantly elevated in cancer samples depending on Fuhrman grade of the disease and PBRM1 status. The olaparib treatment of renal cancer cell lines reduces colony formation and its density exclusively in CAKI-1 cell line obtained from ccRCC metastasis.

Conclusions: ccRCC feature by BRCA1 and CTCF downregulation/loss on protein, but not on transcript level. No common mutation in BRCA1/2 was found. As HR DSB repair is affected the olaparib could be a novel therapeutic approach in metastatic ccRCC treatment.

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