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The centrosomal protein, TAX1 binding protein 2 (TAX1BP2) regulates the chemo-sensitivity of liver cancer cells

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Background: The centrosomal protein, TAX1 binding protein 2 (TAX1BP2) was first identified as a cellular interacting partner of HTLV-I virus oncoprotein, TAX1. Further investigation has shown that TAX1BP2 was targeted by TAX1 to induce supernumerary centrosome in TAX1-expressing cells. Recently, TAX1BP2 was found to be frequently underexpressed in hepatocellular carcinoma (HCC) and underexpression of TAX1BP2 suppressed the activation of tumor suppressor p53 in a p38 MAPK dependent manner, suggesting that TAX1BP2 is a putative tumor suppressor in HCC. Here we provide evidence that TAX1BP2 is also involved in the chemo-sensitivity of HCC cells.
Material and Methods: The protein level of TAX1BP2 in chemo-drug treated HCC cells detected by Western Blotting. In vitro kinase and ubiquitination assays were used to detect phosphorylation and ubiquitination of TAX1BP2 by ATM kinase.,
Result: Upon treatment with chemotherapeutic drugs cisplatin and etoposide, we observed that the level of TAX1BP2 was significantly accumulated in HCC cells. To understand the role of TAX1BP2 in chemo-sensitivity, we found that TAX1BP2 is a phosphorylation substrate of ATM kinase, which plays an important role in DNA damage response. Our result indicated that he phosphorylation of TAX1BP2 by ATM not only stabilized the TAX1BP2 protein via suppressing the ubiquitination proteasomal degradation of TAX1BP2, but also promoted the tumor suppressor activity of TAX1BP2.
Conclusion: TAX1BP2 is a novel substrate of ATM kinase and can potentially be a target for the enhancement of HCC cell chemo-sensitivity.