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Jab1-siRNA induces cell growth inhibition and cell cycle arrest in gall bladder cancer cells via targeting Jab1 signalosome

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The aberrant alteration in Jab1 signalosome (COP9 Signalosome Complex Subunit 5) has been proven to be associated with the progression of several carcinomas. However the specific role and mechanism of action of JAB1 signalosome in carcinogenesis of gall bladder cancer (GBC) is poorly understood. In the current study, we have shown that overexpression of JAB1 stimulated the proliferation of GBC cells; whereas down regulation of JAB1 by using JAB1-siRNA approach resulted in the cell growth inhibition and apoptotic induction. Furthermore, we found that down regulation of Jab1 induces the cell cycle arrest at G1 phase and up regulated the expression of p27, p53 and Bax gene. Moreover, JAB1-siRNA induces apoptosis by enhancing ROS generation and caspase-3 activation. In addition, combined treatment with JAB1-siRNA and gemicitabine demonstrated an enhanced decline in cell proliferation which further suggested increased efficacy of gemcitabine at a very lower dose (5μM) in combination with Jab1-siRNA. In conclusion, our study strongly suggests that targeting Jab1 signalosome could be a promising therapeutic target for the treatment of gall bladder cancer.