HCRP1

Hepatocellular carcinoma-related protein 1 (HCRP1), also known as the homologue of vacuolar protein sorting 37A (hVps37A), serves as a membrane trafficking complex to mediate internalization and degradation of a ubiquitination of membrane receptors.

It is downregulated in several tumors and strongly affects the outcomes of cancer patients. It is reported the expression of HCRP1 is inversely related to epidermal growth factor receptor (EGFR) in breast cancer and lead to resistance to cetuximab in ovarian cancer. However, its exact mechanism in the progression of Hepatocellular carcinoma (HCC) remains unknown.

HCRP1 expression and its clinical significance were examined in 101 HCC patients using immunohistochemistry. Cell proliferation, migration and invasion assays were conducted in HCC cell lines. EGFR activation and degradation were then observed after EGF inducing in HCRP1 knockdown HepG2 cells. In addition, we also detected whether epithelial-to-mesenchymal transition (EMT) was involved in the malignancy promoted by HCRP1. The results showed that 59 of the 101 HCC cases exhibited downregulation of HCRP1 expression ($P<0.01$) as compared to 30 benign liver lesions and 20 normal liver tissues, all of which showed a high level of HCRP1. HCRP1 expression was significantly related to age ($P=0.017$), pathological grade ($P=0.003$), tumor encapsulation ($P=0.037$), recurrence ($P=0.039$) and death ($P=0.015$), but unrelated to cirrhosis ($P=0.216$), tumor size ($P=0.273$), and distant metastasis ($P=0.554$). Lower HCRP1 expression was correlated with shorter RFS and OS ($P<0.001$), and decreased HCRP1 level is an independent prognostic marker in HCC patients ($P<0.05$). Overexpression of HCRP1 decreased and knockdown increased HCC cell proliferation, migration and invasion. HCRP1 depletion increased EGFR activation and inhibited EGFR degradation. EMT phenotype was promoted after HCRP1 downregulation via increase of Snail and Twist1 and activation of Akt phosphorylation in HepG2 cells. Conversely, upregulation of HCRP1 in SMMC-7721 cells led to the opposite effect. In conclusion, our study indicated that downregulation of HCRP1 is a valuable prognostic factor involved in EGFR regulation and acquisition of the mesenchymal phenotype of HCC cells [1)].

In a study, Xu et al. detected the expression pattern of HCRP1 in glioma. The results showed that HCRP1 was significantly down-regulated in glioma tissues and cell lines. On the basis of further analysis, they demonstrated that up-regulation of HCRP1 efficiently inhibited glioma cell proliferation and invasion in vitro, and as well as suppressed glioma cell growth in vivo. In addition, they found that HCRP1 up-regulation decreased the levels of p-ERK and p-AKT in glioma cells. They also emphasized that the ERK and AKT signaling pathways were the mechanisms underlying the inhibitory effect of HCRP1 on glioma cells. Taken together, they provided evidence in support of the prognostic value of HCRP1 in glioma and suggested it as a promising target for glioma treatment [2)].

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2)
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