PTEN Expression Affects the Outcome of Human Hepatocellular Carcinoma via Modulating the Oncogenic Behaviors and the angiogenic Processes

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ABSTRACT BODY:
Reduced phosphatase and tensin homolog (PTEN) expression is associated with vascular endothelial growth factor (VEGF) overexpression in various malignancies. Herein, we aimed to investigate the expression of PTEN and VEGF in *pericancerous* tissues and their association in hepatocellular carcinoma (HCC). PTEN expression was reduced in 43% and VEGF was overexpressed in 31% of 113 resected HCC clinical specimens. VEGF overexpression is positively correlated with young age, male gender, hepatitis B viremia, high α-fetoprotein levels, decline in PTEN expression, advanced tumor stage, and dedifferentiation of HCC. Survival analysis revealed that reduced PTEN expression, microvessel density, and advanced tumor stage were independent poor prognostic factors for disease-free survival. Adenovirus-mediated restoration of PTEN inhibited cell proliferation, clonogenic growth and invasive capability of PTEN-deficient human HCC cells *in vitro*. In xenograft model, PTEN gene delivery could efficiently suppress the incidence and growth rate of implanted tumor cells and reduce microvessel density. The expression of VEGF and HIF1a, and secreted IL-8 were decreased in PTEN restored HCC cells. Angiogenic networks of human umbilical vein endothelial cells were also suppressed by the increased PTEN *in vitro*. *Conclusion:* The tumor microenvironment may be affected by PTEN expression through modulating the oncogenic phenotypes of tumor cells and having a tendency to interfere in angiogenic processes, including expression of angiogenic factors and formation of angiogenic networks. The expression of PTEN and VEGF affecting the outcomes of HCC patients might serve as good prognostic biomarkers.