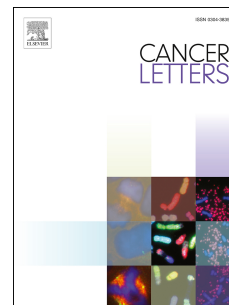


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Cholesterol inhibits hepatocellular carcinoma invasion and metastasis by promoting CD44 localization in lipid rafts

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Abstract

Cholesterol plays a vital role in modulating the action of membrane proteins critical to cellular function. The effect of serum cholesterol on prognosis of hepatocellular carcinoma (HCC) patients is still uncertain. Here, we report that high levels of cholesterol predicts good survival and low disease recurrence after surgery. Cholesterol could significantly suppress migration and invasion of HCC cells, and restrain metastasis of HCC in mice. High levels of cholesterol promoted CD44 translocation into lipid rafts, and attenuated CD44-Ezrin binding, which were crucial for cell migration and cancer metastasis. The suppressive effect of cholesterol on HCC metastasis was abolished by down-regulation of CD44 or its palmitoylation inhibitor, which blocked CD44 localization in lipid rafts. Furthermore, pharmacologically promoting CD44 retention inside lipid rafts obviously attenuated HCC migration and invasion, providing a potential therapeutic strategy to prolong survival of HCC patients.

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