

学位論文の内容の要旨

専攻	医学専攻	部 門 (平成27年度以前入学者のみ記入)	
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論文題目	Evaluating the Effect of Lenvatinib on Sorafenib-Resistant Hepatocellular Carcinoma Cells		
<p>(論文要旨)</p> <p>Hepatocellular carcinoma (HCC) is one of the major causes of cancer-related deaths worldwide. Sorafenib has been used as a first-line systemic treatment for over a decade. However, resistance to sorafenib limits patient response and presents a major hurdle during HCC treatment. Lenvatinib has been approved as a first-line systemic treatment for advanced HCC and is the first agent to achieve non-inferiority against sorafenib. Therefore, in the present study, we evaluated the inhibition efficacy of lenvatinib in sorafenib-resistant HCC cells. Only a few studies have been conducted on this topic. Two human HCC cell lines, Huh-7 and Hep-3B, were used to establish sorafenib resistance, and in vitro and in vivo studies were employed. Lenvatinib suppressed sorafenib-resistant HCC cell proliferation mainly by inducing G1 cell cycle arrest through ERK signaling. Hep-3B sorafenib-resistant cells showed partial cross-resistance to lenvatinib, possibly due to the contribution of poor autophagic responsiveness. Overall, the findings suggest that the underlying mechanism of lenvatinib in overcoming sorafenib resistance in HCC involves FGFR4-ERK signaling. Lenvatinib may be a suitable second-line therapy for unresectable HCC patients who have developed sorafenib resistance and express FGFR4.</p>			

掲 載 誌 名	International Journal of Molecular Sciences 第 22 卷, 第 23 号		
(公表予定) 掲 載 年 月	2021 年 12 月	出版社 (等) 名	MDPI
Peer Review	①		無

(備考) 論文要旨は, 日本語で1, 500字以内にまとめてください。