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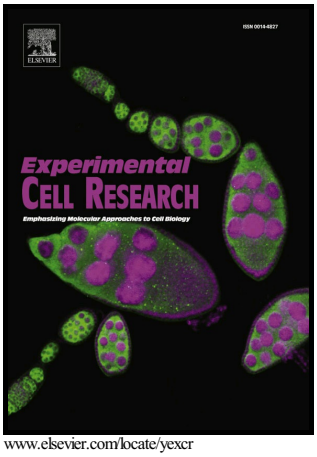


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PII: S0014-4827(18)30834-6
DOI: https://doi.org/10.1016/j.yexcr.2018.09.001
Reference: YEXCR11187

To appear in: *Experimental Cell Research*

Received date: 31 March 2018
Revised date: 29 August 2018
Accepted date: 1 September 2018

Cite this article as: Azemat Jamshidi-Parsian, Robert J. Griffin, Rajshekhar A. Kore, Valentina K. Todorova and Issam Makhoul, Tumor-endothelial cell interaction in an experimental model of human hepatocellular carcinoma, *Experimental Cell Research,* https://doi.org/10.1016/j.yexcr.2018.09.001

# Tumor-endothelial cell interaction in an experimental model of human hepatocellular carcinoma

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## Abstract

Hepatocellular carcinoma (HCC) is a densely vascularized tumor that is highly dependent on angiogenic pathways to direct arterial blood flow to the growing neoplasm, though little is known about how the interaction of tumor and endothelial cells drives these processes and the degree of clinical importance. To this end, we examined the intercellular cross-talk between HepG2 (human HCC) and human endothelial progenitor cells (EPC) in a co-culture system that mimics some aspects of initial tumor parenchyma and stroma interactions. The results showed that the remote cell-to-cell (paracrine) interactions between HepG2 cells and EPC play a critical role in the differentiation and angiogenic activity of endothelial cells, possibly through intercellular signaling function of the exosomes released in the medium by HepG2 cells. The tumor-cell activated phenotype of EPC was associated with increased migration and elevated expression of ephrin-B2, and Delta-like 4 ligand (DLL4). Furthermore, ephrin-B2 was found to be overexpressed in HCC and cholangiocarcinoma tissue samples taken from humans. Overall, our results demonstrate that ephrin-B2 and Dll4 mediated co-dependence of HCC and EPC