Microenvironment and Immunology

Cancer Research

# Comment Re: Lactate-Induced IL-8 Pathway in Endothelial Cells—Letter

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## Abstract

Végran and colleagues proposed a model in which the lactate released from tumor cells through MCT4 would be taken up by endothelial cells via the MCT1 transporter and stimulate angiogenesis, using human umbilical vein endothelial cell (HUVEC) as model of tumor endothelial cells. By analyzing a total of 505 cases of human tumor samples immunostained for MCT1, we do not confirm plasma membrane expression of MCT1 in the endothelial cells of tumor-associated vessels. *Cancer Res; 72(00); 1–2. ©2012 AACR.*

We read with great interest the work of Végran and colleagues published recently (1), where the authors nicely showed, using human umbilical vein endothelial cell (HUVEC) as a model, that lactate induces angiogenesis through NF-κB/interleukin-8 (IL-8) signaling. The entrance of lactate in endothelial cells was shown to be mediated by monocarboxylate transporter MCT1, present in HUVECs. The authors then proposed a model in which the lactate released from tumor cells through MCT4 would be taken up by endothelial cells via the MCT1 transporter and stimulate angiogenesis.

Our group has been studying the expression of MCT1 and MCT4 in several human tumor samples, including colorectal (2), uterine cervix (3), and breast (4), in a total of 505 cases. In the light of the results presented by Végran and colleagues, we checked again all our samples and we did not find any clear MCT1 plasma membrane expression in endothelial cells of blood vessels in any of the tumor samples. Representative pictures of MCT1 immunohistochemistry in the different tumors are shown in Fig. 1, in which negative reactions can be seen in the endothelial cells of blood vessels near tumor cells. We confirmed the specificity of the MCT1 antibody we used for immunohistochemistry, by Western blotting (2) and, most recently, by siRNA (unpublished results), which is the same as the authors used in the present article.

Even though HUVECs have been largely used as an *in vitro* model for tumor angiogenesis, they are isolated from the vein of the umbilical cord and there are evident differences in gene expression between their phenotype and tumor endothelial

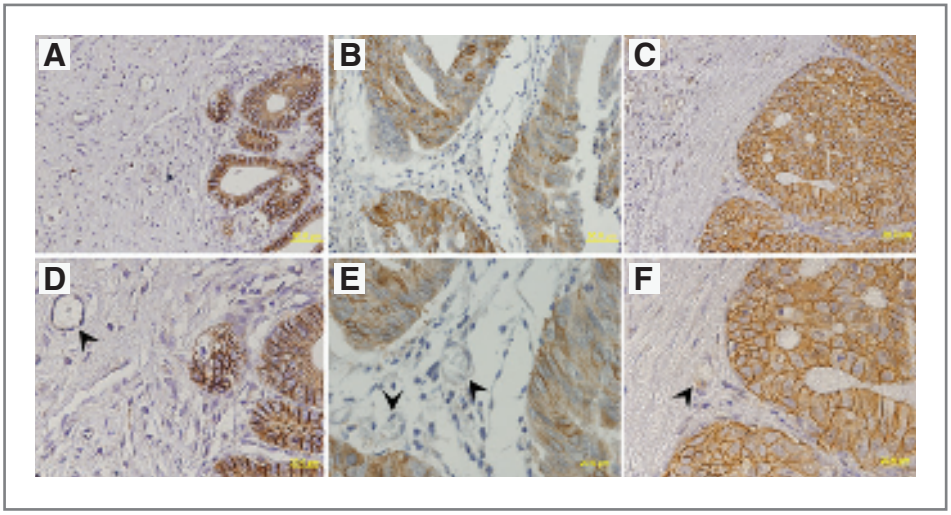


Figure 1. Representative immunoreactions for MCT1 in cervical (A, D), colorectal (B, E), and breast cancer (C, F), where negative staining of endothelial cells in the vicinity of tumor cells can be seen (black arrowheads). A–C, ×200 magnification; D–F, ×400 magnification.

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**doi:** 10.1158/0008-5472.CAN-11-1540

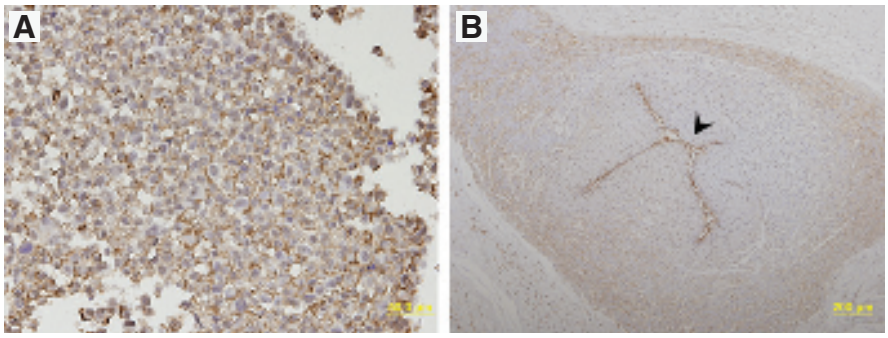


Figure 2. Representative immunoreactions for MCT1 in HUVECs (A) and umbilical cord (B), where positive staining for MCT1 can be seen (black arrowhead).

cells (5), which may also be the case of MCT1. Indeed, by using the same technique, antibody and specimen processing, we see clear expression of MCT1 in HUVECs (Fig. 2) but do not confirm plasma membrane expression of MCT1 in tumor-associated vessels.

We would like to leave the message that one should interpret the results from studies using *in vitro* models with caution, as they might not reflect accurately what happens in human tissues.

## Disclosure of Potential Conflicts of Interest

All the authors confirm that the information reported above is accurate and understand that this information will be disclosed publicly. The *AACR* reserves the right to decline to publish their work if the Association believes a serious conflict of interest exists. They also understand that failure to complete this form will disqualify their manuscript from consideration for publication. No potential conflicts of interests were disclosed. Q5

## Authors' Contributions

Q6

Conception and design: C. Pinheiro, F. Baltazar

Development of methodology: C. Pinheiro, F. Baltazar

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): C. Pinheiro, A. Longatto-Filho, F. Baltazar

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Received May 13, 2011; revised November 9, 2011; accepted November 21, 2011; published OnlineFirst xx xx, xxxx.

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