Lactate Oxidation in Endothelial Cells: A Feature of All Endothelial Cells?

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Metabolism of endothelial cells is a topic that has gained an increasing interest in the last years. This is due to their role in the angiogenic process, which is pathologically upregulated in several diseases, such as retinopathies, diabetes and cancer. Glycolysis, among other metabolic routes, has been found to be essential for triggering the angiogenic switch. Additionally, it has been seen that endothelial cells are able to take up lactate from the extracellular media, for example in the case of the tumor microenvironment, where cancer cells would have secreted high amounts of this metabolite. Endothelial cells would oxidize this lactate for obtaining energy, but lactate can also act as a signaling molecule for the angiogenic process. However, experiments to determine the molecular fate of lactate have been performed using only macrovascular endothelial cells. The aim of the present work is to prove whether microvascular endothelial cells are also able to take up and oxidize lactate. For this purpose, fluorimetry, isotopic labeling and Seahorse experiments were used to study the metabolism of a human microvascular endothelial cell line (HMEC). The expression levels of transcripts and proteins of different enzymes and transporters related to lactate metabolism were estimated by qPCR and Western blotting. The results obtained indicate that these cells rely on glycolysis for their metabolism, while the oxidation of glucose and glutamine seems to be considerably low. On the other hand, no lactate oxidation could be detected. We then checked the mRNA expression of the two isoenzymes of lactate dehydrogenase (LDH) and the two main lactate transporters, MCT1 and MCT4, and found that levels of LDH-B and MCT1 were undetectable. We failed to measure any MCT1 mRNA or protein expression either in normoxia or hypoxia. Hence, we can conclude that at least this microvascular endothelial cell line cannot use extracellular lactate as a metabolic fuel.

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