Development of Molecular Tools for Expression and Trafficking Studies of The Human Monocarboxylate Transporters

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Most cancer cells rely on glycolysis to sustain their high proliferation rates with the production of lactate. For many years, lactate was seen as a metabolic waste of glycolytic metabolism in the tumor microenvironment, however, lactate has been recently associated as a key metabolic fuel and as an important signaling molecule 1,2. This substrate is responsible for extracellular acidification, which, is a feature of the tumor environment, and favors tumor invasion. The transport of lactate across the plasma membrane is mediated by a family of proton coupled monocarboxylate transporters (MCTs), which comprises 14 members 3. MCT1 and MCT4 serve as metabolic links between cancer cells via lactate exchange within tumors. This form of metabolic symbiosis illustrates how the apparent waste product from hypoxic tumor cells may be exploited by oxidative tumor cells to sustain their energy production under nutrient deprived conditions 4. MCTs are not only gatekeepers of intercellular metabolic cooperation, but also important regulators of angiogenesis and tumor migration, invasion and metastasis 5 . However, the role of MCTs in tumors is far from being well understood and their potential as therapeutic targets is poorly explored. Given the relationships between MCT1 and MCT4 in cancer cells, they offer a unique opportunity for novel treatment strategies.

In this work, a set of molecular tools was generated for the expression and trafficking analyses of MCT1 and MCT4. Plasmids were designed harboring MCT1 or MCT4 with GFP or mCherry at the C- or N- terminal following the classical DNA cloning method. These molecular tools will be essential to study the expression and localization of MCT1 and MCT4 and to study the conditions and mechanisms underlying the endocytic trafficking of both transporters to further elucidate the significance of MCTs expression in tumor cells.

Keywords:

Cancer, lactate, metabolic reprograming, monocarboxylate transporters, MCT1, MCT4, molecular cloning.

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