Glucose Metabolism and Aberrant Glycosylation during Epithelial Mesenchymal Transition: Role of O-GlcNAc

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Deregulated cellular metabolism is a hallmark of tumors. Several studies have been focused in importance glycolysis and pentose phosphate pathway. However, a neglected but very important branch of glucose metabolism is the hexosamine biosynthesis pathway (HBP). The HBP is a branch of the glucose metabolic pathway that consumes approximately 2–5% of the total glucose, generating UDP-GlcNAc as end-product. UDP-GlcNAc is the donor substrate used in multiple glycosylation reactions such as O-GlcNAcylation. Here, we investigate the changes of glucose metabolism during epithelial and mesenchymal transition (EMT), and the role of O-GlcNAcylation in this process. We show that A549 cells increase the glucose uptake during EMT, but instead of increase the glycolysis and PPP, the glucose is shunted though the HBP.The activation of HBP induces an aberrant cell surface glycosylation and O-GlcNAcylation. The cell surface glycansdysplays the increase of sialylation α2-6, poly-LacNAc and fucosylation, all known epitopes found in different tumor models. In addition, modulation of O-GlcNAc levels was demonstrated to be important during EMT process. Taken together, our results indicates that EMT is an applicable model to study metabolic and glycophenotype changes during carcinogenesis, indicating that cell glycosylation senses metabolic changes and modulates cell plasticity.

Keywords: Glycosylation, cancer and glucose metabolism