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EFFECTS OF ARHGAP21 SILENCING ON GENE EXPRESSION IN PROSTATE ADENOCARCINOMA CELL LINES: ALTERATION OF GLYCOLYSIS CANONICAL PATHWAY

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ARHGAP21 is a RhoGAP protein that interacts to FAK, PKC zeta, alfa-catenin and ARF-1, linking RhoGTPases to other signaling pathways. ARHGAP21 inhibits glucose-stimulated insulin secretion and its interactions with FAK and PKC zeta is modulated by glucose. Here, we aimed to study the roles of ARHGAP in glycolysis pathway and hypoxia process in LNCaP, and other prostatic carcinoma cells: PC-3 and DU145 cells control and submitted to ARHGAP21 inhibition. Specific siRNAs targeting ARHGAP21 were used to inhibit ARHGAP21 expression in LNCaP, PC-3 and DU145 (siARHGAP21 cells). Microarray assays were performed in LNCaP cells, using Human Gene (Affymetrix) platforms. The expression of some genes related to hypoxia and glycolysis was evaluated by qRT-PCR in the same cells. Was found that ARHGAP21 inhibition modulated the expression of twelve genes related to hypoxia or glycolysis. qRT-PCR confirmed HIG2, PGAM, BNIP3 and Stanniocalcin up-regulation in LNCaP siARHGAP21. BNIP3 was also up-regulated in PC-3 cells siARHGAP21. PLOD2 expression was down-regulated in LNCaP and DU145 cells siARHGAP21, whereas HK2 was downregulated in LNCaP and upregulated in DU145 siARHGAP21. It is know that solid tumours are poorly oxygenated and require high taxes of glucose. Therefore, ARHGAP21 might be involved in the adaptation of tumor cells in the hypoxic environment and increased glucose uptake.

ARHGAP21 - Glycolysis - Hypoxia