An Exploratory Investigation of microRNA Regulation of ACSL4 in Androgen Deprivation Therapy Resistant Prostate Cancer

Du, Xinxin

One prominent treatment for prostate cancer is androgen deprivation therapy, which slows tumor growth by targeting the androgen receptor signaling pathway. Unfortunately, most tumors progress to a resistant, androgen independent state. Previous studies have indicated that altered lipid metabolism is involved in prostate cancer. The present study further investigated the role of one lipid metabolic enzyme, long-chain fatty acyl-CoA synthetase 4 (ACSL4) in prostate cancer in relation to androgen deprivation therapy. Our results suggest that ACSL4 is linked to many aspects of androgen deprivation therapy resistance. ACSL4 was implicated in androgen independence, malignant transformation, and dysregulation of cell cycle and apoptosis regulating pathways. These results suggest that ACSL4 might be useful as a biomarker to guide patient treatment options or as a possible target for future pharmacological therapies. One area of further investigation was looking into microRNA level post transcriptional regulation of ACSL4. Two microRNA, microRNA 421 and microRNA 34a were identified as possible regulators of ACSL4 using the binding prediction program TargetScan.. A negative correlation between microRNA 34a and aggressive phenotype was seen comparing microRNA 34a levels across the cell lines used. Cells treated with microRNA 421 mimic did not show statistically significant ACSL4 silencing compared with the scrambled control. Cells treated with microRNA 34a mimic did not show statistically significant ACSL4 silencing compared with the scrambled control. Understanding microRNA level regulation of growth in prostate cancer could lead to the development of blood based microRNA biomarkers and microRNA pharmacological therapies.

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