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Abstract

Cucurbitacin D: An Innovative Approach for Metastatic Prostate Cancer Treatment

Mohammed Sikander[1,2], Shabnam Malik[1,2], Subhash C. Chauhan[1,2], Meena Jaggi[1,2]*

[1] Department of Immunology and Microbiology, School of Medicine, University of Texas Rio Grande Valley, McAllen, TX 78504, USA
[2] South Texas Center of Excellence in Cancer Research, School of Medicine, University of Texas Rio Grande Valley, McAllen, TX 78504, USA

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Abstract

Background and aim: Prostate cancer (PrCa) is one of the most common cancers in men and the second leading cause of cancer deaths in the United States. Emergence of castration resistant PrCa and chemo-resistance are some of the major hurdles in managing PrCa. Accumulating evidence has shown that higher glucose uptake is required for rapid proliferation of androgen-insensitive PrCa cells. Notably, natural compounds can modify glucose uptake by altering GLUT1 expression and/or glucose binding. Herein, we investigated in vitro and in vivo model systems to assess the therapeutic efficacy and underlying molecular mechanisms of Cuc D against PrCa.

Materials and methods: The anticancer effect of Cuc D on GLUT1 and associated signaling mechanisms in prostate cancer was investigated using proliferation, clonogenicity, migration, invasion, Western blotting, and qPCR analysis. Glucose and Lactate assays were performed in prostate cancer cells using kits purchased from Cayman Chemical.

Results: Our experimental findings indicated that Cuc D not only inhibits the proliferation and invasion of prostate cancer cells but also modifies the glucose uptake and lactate secretion of these cells. Treatment with Cuc D induces apoptosis and causing the cells to arrest in the G2/M phase of the cell cycle in human prostate cancer cells. This metabolic shift caused by Cuc D was found to have a correlation with a decrease in the expression of GLUT1 caused by its direct binding, as evidenced by its efficient molecular docking. In the PrCa xenograft mouse model, treatment with Cuc D demonstrated a suppression of tumor growth, which coincided with a concurrent decrease in the expression of GLUT1 and PCNA and a restoration of miR-132.

Conclusion: Based on these findings, Cuc D has the potential to be a novel modulator of glucose metabolism as well as a potentially useful for the prevention of prostate cancer.

Keywords: *Cucurbitacin D, Innovative Approach, Metastatic Prostate Cancer*

***Corresponding author:** Meena Jaggi, Department of Immunology and Microbiology, School of Medicine, University of Texas Rio Grande Valley, McAllen, TX 78504, USA; South Texas Center of Excellence in Cancer Research, School of Medicine, University of Texas Rio Grande Valley, McAllen, TX 78504, USA.
E-mail address: meena.jaggi@utrgv.edu