Molecular Insights into Targeting PKD1 for Prostate Cancer Treatment

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Background: Prostate cancer has a poor prognosis due to late diagnosis and ineffective multimodal clinical treatment. Efforts are underway to create strategies for resolving the abnormal expression of molecular targets implicated in disease development and progression. We previously reported that the serine threonine kinase Protein Kinase D1 (PKD1) regulates a multitude of tumor suppressor functions, including cell aggregation, motility, proliferation, and invasion in prostate cancer. Thus, PKD1 is regarded as a promising therapeutic target for the treatment of prostate cancer.

Objective: The goal of this study was to investigate the therapeutic potential of ormeloxifene (ORM), a pharmacological modulator with well-defined PK/PD and safety profiles in humans, for PKD1 restoration in prostate cancer.

Methods: The anticancer effect of ORM on PKD1 and associated signaling mechanisms in prostate cancer was investigated using proliferation, clonogenicity, migration, invasion, western blotting, and qPCR analysis.

Results: In comparison to the vehicle-treated group, ORM treatment decreased prostate cancer cell proliferation, invasion, migration, and colony formation in a dose-dependent manner. In C4-2 cells, ORM treatment selectively induces PKD1 expression at both the mRNA and protein levels. Furthermore, our findings revealed that ORM efficiently suppresses MTA1 expression in prostate cancer cells. MTA1 physically interacts with PKD1 and has been shown to have an inverse correlation with it. Our results also showed that ORM treatment enhances the therapeutic efficacy of decetaxel.

Conclusion: Taken together, these findings show that ORM has anticancer properties in prostate cancer *via* restoring PKD1.