

## **The relationship between Circumcision and Human Papillomavirus infection: A Systematic Review and Meta-Analysis**

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**BACKGROUND:** CDKN3 (cyclin-dependent kinase inhibitor 3) belongs to the protein phosphatases family. Despite the importance of CDKN3 in tumorigenesis, how CDKN3 plays a role and the regulated mechanism in prostate cancer ( Pca) is largely unknown.

**HYPOTHESIS:** CDKN3 plays an important role in prostate cancer, and may act as a potential new therapeutic target for treatment of prostate malignancies.

**METHODS:** We first assayed the expression of CDKN3 in PCa tissue samples and PCa cell lines by real-time PCR and western blotting. We then defined the biological functions of CDKN3 by CCK-8 assay, flow cytometry and transwell assay. We used Gene set enrichment analysis (GSEA) of KEGG dataset to probe the CDKN3-associated pathways and confirmed the findings from GSEA by Western blotting. Nude mouse xenograft experiment was performed to assay the effect of CDKN3 down-regulation on tumor growth.

**RESULTS:** CDKN3 expression was markedly increased in prostate cancer tissues and prostate cancer cell lines LNCap and PC3. Moreover, down-regulation of CDKN3 inhibited cell proliferation, induced a G1 phase arrest in cell cycle, inhibited cell invasion and promoted cell apoptosis in LNCap and PC3 cells. GSEA showed that cell cycle and DNA replication signaling were correlatively with CDKN3 expression. Western blot results showed that the expression levels of cell cycle related proteins PCNA and CDK1 were down-regulated and DNA replication related proteins MCM2 and MCM3 were also reduced. Finally, in vivo data showed that knockdown of CDKN3 expression dramatically inhibited the prostate tumor growth in nude mouse. Our data suggest an important role of CDKN3 in the molecular etiology of prostate cancer and implicate the potential application of CDKN3 in prostate cancer therapy.