



# Snake (*Walterinnesia aegyptia*) venom-loaded silica nanoparticles induce apoptosis and growth arrest in human prostate cancer cells.

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## Abstract:

Prostate cancer (PCa) is the most commonly diagnosed cancer in men. The progression and invasion of PCa are normally mediated by the overexpression of chemokine receptors (CKRs) and the interaction between CKRs and their cognate ligands. We recently demonstrated that venom extracted from *Walterinnesia aegyptia* (WEV) either alone or in combination with silica nanoparticles (WEV+NP) mediated the growth arrest and apoptosis of breast cancer cells. In the present study, we evaluated the impact of WEV alone and WEV+NP on the migration, invasion, proliferation and apoptosis of prostate cancer cells. We found that WEV alone and WEV+NP decreased the viability of all cell types tested (PCa cells isolated from patient samples, PC3 cells and LNCaP cells) using an MTT assay. The IC(50) values were determined to be 10 and 5  $\mu$ g/mL for WEV alone and WEV+NP, respectively. WEV+NP decreased the surface expression of the CKRs CXCR3, CXCR4, CXCR5 and CXCR6 to a greater extent than WEV alone and subsequently reduced migration and the invasion response of the cells to the cognate ligands of the CKRs (CXCL10, CXCL12, CXCL13 and CXCL16, respectively). Using a CFSE proliferation assay, we found that WEV+NP strongly inhibited epidermal growth factor-mediated PCa cell proliferation. Furthermore, analysis of the cell cycle indicated that WEV+NP strongly altered the cell cycle of PCa cells and enhanced the induction of apoptosis. Finally, we demonstrated that WEV+NP robustly decreased the expression of anti-apoptotic effectors, such as B cell Lymphoma-2 (Bcl-2), B cell Lymphoma-extra large (Bcl-XL) and myeloid cell leukemia sequence-1 (Mcl-1), and increased the expression of pro-apoptotic effectors, such as Bcl-2 homologous antagonist/killer (Bak), Bcl-2-associated X protein (Bax) and Bcl-2-interacting mediator of cell death (Bim). WEV+NP also altered the membrane potential of mitochondria in the PCa cells. Our data reveal the potential of nanoparticle-sustained delivery of snake venom as effective treatments for prostate cancer.

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