Vacuolar ATPases (V-ATPases) comprise specialized and ubiquitously distributed pumps that acidify intracellular compartments and energize membranes.

The role of V-ATPases in prostate cancer (PCa), was studied by inhibiting V-ATPase pumps in androgen-dependent (LNCaP) and androgen-independent (C4-2B) cells of a human PCa progression model.

Treatment with nanomolar concentrations of the V-ATPase inhibitors bafilomycin A (Baf.A) or concanamycin A (Conc.A) reduced the in vitro invasion in both cell types by 80%, regardless that V-ATPase was prominent at the plasma membrane of C4-2B cells and only traces were detected in the low-metastatic LNCaP parental cells.

The V-ATPase inhibitors, additionally, interfered with the AR-PSA axis under conditions that reduced invasion. Bafilomycin A significantly reduced steady-state and R1881-induced PSA mRNA expression and secretion in the LNCaP cells which are androgen-dependent, but not in the C4-2B cells which are androgen ablation-resistant. In the C4-2B cells, an increased susceptibility to V-ATPase inhibitors was detected after longer treatments, as proliferation was reduced and reversibility of bafilomycin-induced responses impaired.

These findings make V-ATPases attractive targets against early and advanced PCa tumors.