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Abstract

CAVPENET Decreases Prostate Cancer Cells Proliferation and Invasion through Modulation of Protein Phosphatase Activity †

Bárbara Matos [1,2], John Howl [3], Carmen Jerónimo [2,4] and Margarida Fardilha [1,*]

[1] Laboratory of Signal Transduction, Department of Medical Sciences, Institute of Biomedicine iBiMED, University of Aveiro, 3810-193 Aveiro, Portugal; barbaracostamatos@ua.pt
[2] Cancer Biology and Epigenetics Group, IPO Porto Research Center (CI-IPOP), Portuguese Institute of Oncology of Porto (IPO Porto), Research Center-LAB 3, F Bdg., 1st floor, Rua Dr. António Bernardino de Almeida, 4200-072 Porto, Portugal; carmenjeronimo@ipoporto.min-saude.pt
[3] Molecular Pharmacology Group, Research Institute in Healthcare Science, University of Wolverhampton, Wolverhampton WV1 1LY, UK; j.howl@wlv.ac.uk
[4] Department of Pathology and Molecular Immunology, Institute of Biomedical Sciences Abel Salazar, University of Porto (ICBAS-UP), Rua Jorge Viterbo Ferreira 228, 4050-513 Porto, Portugal
* Correspondence: mfardilha@ua.pt
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Abstract: Despite advances in understanding the molecular mechanisms underlying prostate cancer progression, the development of effective therapeutic approaches remains a major challenge. In this context, the protein phosphatase 1 (PP1) and its complexes have been recognized as potential drug targets. Herein, we designed and synthetized a peptide sequence based on the PP1-binding motif of CAV1, which was coupled with penetratin to improve cellular uptake. To evaluate the effect of the synthetized peptide, named CAVPENET, prostate cancer cells (PC-3 and LnCaP) were incubated with CAVPENET for 48 h, and several parameters were analyzed. We found that CAVPENET significantly decreased the LnCaP and PC-3 cells viability and invasive ability. A significant decrease in the phosphorylation of AKT at Ser^{473} was also observed after 48 h of incubation with CAVPENET. Moreover, a slight recovery of AKT phosphorylation levels after the simultaneous incubation of CAVPENET (10 µM) with tautomycin (10 nM)—a highly specific PP1 inhibitor—suggested the role of PP1 in the CAVPENET-induced alterations in AKT phosphorylation. Moreover, incubation with CAVPENET (10 µM) + cantharidin (0.5 µM), a potent and selective PP2A inhibitor, almost completely recovered the phosphorylation levels of AKT, suggesting the role of PP2A in the effect of CAVPENET. Altogether, these results highlight the potential of the synthesized peptide to negatively impact the PCa cells' proliferation and invasive ability by interfering with the interaction of CAV1 with PP1 and/or PP2A. Further analyses are now required to confirm the disruption of the interactions and to better elucidate the mechanisms of cell death.

Keywords: prostate cancer; PP1; PP2A; peptide; phosphatase; CAV1

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