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Abstract topic: Cellular Pathology

Title: CAVPENET decreases prostate cancer cells proliferation and invasion through modulation of protein phosphatase activity

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Abstract (150-300 words):

Prostate cancer (PCa) is a disquieting cause of men's death worldwide and there is an urgent need to develop new effective therapeutic strategies. Protein phosphatase 1 (PP1) recently emerged as a promising therapeutic target in cancer. In this context, the main goal of this work is to develop peptides to disrupt a key PP1 complex for PCa development, thus impairing PCa progression. The peptide designed to interrupt the interaction between PP1 and caveolin-1 (CAV1) was synthetised using microwave-assisted solid phase synthesis and coupled to penetratin to allow an efficient cell delivery. The efficacy of the synthetised peptide - CAVPENET (and a scrambled homologue - CAVPENET control) was evaluated *in vitro*, using androgen-dependent (LnCaP) and androgen-independent (PC-3) cell lines. We found that, after 48h incubation, CAVPENET significantly

decreases the LnCaP and PC-3 cells viability and invasive ability. A significant decrease in the phosphorylation of AKT at Ser473 was also observed after 48h incubation with CAVPENET. A slightly recover of AKT phosphorylation levels after simultaneously incubation of CAVPENET (10 μM) with tautomycin (10nM) – a highly specific PP1 inhibitor, suggested a role of PP1 in the CAVPENET-induced alterations in AKT phosphorylation. Moreover, incubation with CAVPENET (10μM) + Cantharidin (0.5μM) – a potent and selective PP2A inhibitor, almost completely recover the phosphorylation levels of AKT, suggesting a role for PP2A in the effect of CAVPENET. Altogether, these results highlight the potential of the synthetised 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 cells death.