

**Effects of CPP-conjugated ER $\alpha$ 17p peptide derivatives on the activation of ERK1/2 in breast carcinoma cells**

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The molecule ER $\alpha$ 17p is an estrogenic peptide (sequence: H<sub>2</sub>N-PLMIKRSKKNLALSALT-OH) that exerts its action through conventional nuclear pathways, according to the following process: (i) interaction with the estrogen receptor ER $\alpha$ , (ii) dimerization / phosphorylation, (iii) recruitment of coactivators, and, *in fine*, (iv) interaction with estrogen-response elements (EREs). It acts also through membrane-initiated signalling events, including the membrane estrogen receptor and the heptatransmembrane G protein-coupled receptor GPR30. In steroid-deprived conditions, it activates ERK1/2, the redistribution of actin, transcription, and cell proliferation.

We have studied the effects of this peptide alone or conjugated to the cell-penetrating peptides (CPPs) Arg<sub>9</sub>, RW9 and penetratin on ERK1/2 phosphorylation, on the redistribution of actin, and on cell proliferation in ER $\alpha$ -positive human MCF-7 breast carcinoma cells. We have also quantified the amount of internalized peptide by using MALDI-TOF.

We show here that the penetratin-ER $\alpha$ 17p conjugate enters cells much more efficiently than the other CPP conjugates. Moreover, this conjugate strongly modifies the distribution and the density of actin, and induces the loss of some of the morphological characteristics related to cell proliferation and invasiveness. Also, it is responsible for a decrease in cell proliferation at 48h and 72h.