The Na^{+}/Ca^{2+} Exchanger Inhibitor Peptide Interacts with Glycosaminoglycans at Cell Surface and Belong to Family of Cell Penetrating Peptide.

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Here, we show that the Na+/Ca2+ Exchanger Inhibitor Peptide, XIP (RRLLFYKYVYKRYRAGKQRG) belongs to the family of cell penetrating peptides (CPPs). In order to elucidate the cellular mechanism of XIP penetration, its interaction with glycosaminoglycans (GAG) was studied. The interaction of XIP with GAGs was monitored by affinity chromatography, fluorescence spectroscopy and by far UV-CD spectroscopy analysis. The cellular uptake of XIP was studied in CHO-K1 cells and in their mutants deficient in all cellular GAGs, CHO-745 cells. Intracellular localization and cellular trafficking of FITIC-XIP was monitored using a confocal laser scanning microscope. The data shows that among GAGs tested only heparin and heparan sulfate showed a high affinity binding to XIP. CD analysis suggest that heparin and heparin fragments induces a significant amount of β-sheet on XIP. The mechanism of FITIC-XIP penetration into CHO cells shows the involvement of GAGs in the uptake phase, which is followed by endocytosis and peptide accumulation within the acidic endosomal/lysosomal vesicles. Finally, the permeabilization of endosomal membranes induced by XIP results in the leakage of the vesicles contents to the cytoplasm. Also, the cytotoxicity effect of XIP is related to its endocytosis mechanism. (Supported by CAPES, CNPq and FAPESP).