Synthesis and studies on the cell-penetrating ability of fusogenic peptide for the delivery of ODN or siRNA

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The efficiency of either antisense oligonucleotides (ODN) or siRNAs as gene inhibiting agents is limited by they poor ability to cross cell membranes. The selection of agents which facilitate the cellular delivery is therefore a challenge for antisense strategies. Fusogenic peptides, often involved into virus cell uptake, are goods candidates for this application because they are able to interact efficiently with cell membranes and then to make penetrate large complexes. Generally fusogenic compounds are covalently linked to the nucleic acids but need chemical modifications. In this study we have compared the ability of different peptides to deliver nucleic acids into cells after electrostatic complexes formation. We have synthesized peptides derived from antenapedia, FHV, SV40 signal peptide and their fluorescent coumarin labeled derivative. ODNs and peptides interaction was studied by circular dicroism spectroscopy. Taking advantage of the fluorescence labeling we have studied by epifluorescence microscopy their ability to interact with cultured cells and then to efficiently make penetrate ODNs.