

P012 Cellular Delivery of siRNA by a non-covalently attached peptide: quantitative analysis of uptake and biological effect.

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Oligomeric nucleic acids like siRNAs can only be employed as therapeutics if an appropriate carrier system is available to translocate them into cells to reach their targets. Carrier peptides, acting as shuttles for a controlled delivery, represent an innovative concept to bypass the problem of low bioavailability of nucleic acids. Consequently, the intracellular transport of these compounds is of major importance for new therapeutic concepts. In this study we focused on the quantification of siRNA uptake mediated by a carrier peptide termed MPG α . This peptide forms non-covalent complexes with oligonucleotides which translocate into mammalian cells. The amount of siRNA internalized was quantified using a liquid hybridization assay. Furthermore, the mechanism of the uptake was investigated using fluorescence microscopy and inhibitors of endocytotic pathways. Live-cell fluorescence images and effects of various inhibitors on cellular uptake show that MPG α /siRNA complexes enter cells via an endocytotic pathway. Eventhough the siRNA effect observed using MPG α as carrier is as good as with Lipofectamine 2000, larger amounts of siRNA have to be applied. That may be due to an inferior endosomal escape or decaging and is the focus of further investigations.