

**P022** Peptidomimetics with  $\beta$ -peptoid residues for delivery of siRNA

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Due to their high specificity and potency, small interfering RNA's are recognized as promising drug candidates for gene silencing. However, the delivery of siRNA is hampered by the physico-chemical characteristics. A novel type of peptidomimetics consisting of alternating repeats of  $\alpha$ -amino acid and  $\beta$ -peptoid residues have been found to possess antimicrobial and membrane destabilizing effects as a result of their different side groups<sup>1</sup> and are explored for assessment of intracellular delivery of siRNA to the cytoplasm.

Studies showed that fluorescein-labelled peptidomimetics were efficiently taken up by HeLa cells in a punctuated pattern that was especially evident for the peptidomimetics with a guanidinium side group as compared to an amine group. Compared to the corresponding  $\alpha$ -peptide, the  $\beta$ -peptidomimetics were taken up much more efficiently. However, silencing of the EGF protein expression was not obtained when administering simple mixtures of peptidomimetics and siRNA to HeLa cells stably expressing EGFP, which probably is due to poor serum stability or cellular internalization. The effect of siRNA-peptidomimetic particulate complexes and covalently coupled siRNA-peptide potentially encapsulated in a drug delivery system<sup>2</sup> is currently ongoing.

<sup>1</sup>Olsen, C.A. et al. submitted, <sup>2</sup>Foged et al. 2007.