

P015 CADY: a new generation of secondary amphipathic peptides for the delivery of siRNA

**A. Charnet¹, L. Crombez¹, G. Aldrian-Herrada¹,
R. Bresseur², F. Heitz¹ and G. Divita¹**

¹CRBM-CNRS, Dpt of Molecular Biophysics & Therapeutics, Montpellier, France; ²CBMN-FSAGx, Gembloux, Belgium

The dramatic acceleration in the identification of new nucleic acid-based therapeutic molecules has provided new perspectives in pharmaceutical research. RNA interference has become the method of choice to suppress gene expression both *in vitro* and *in vivo*. However, development of these molecules is limited by poor cellular uptake and cellular trafficking. **In order to improve** cellular uptake of siRNA, we have designed a short secondary amphipathic peptide (CADY) of 17 residues combining aromatic tryptophan and cationic arginine residues. CADY-carrier adopts a helical conformation within cell membranes, whilst exposing charged residues on one side, and Trp-groups that favor cellular uptake on the other. **We have demonstrated that CADY-peptide** forms stable complex with siRNA, through non-covalent interactions, thereby increasing their stability and **efficiently improving** their delivery into a wide variety of cell lines, including suspension and primary cell lines. **CADY-carriers were applied to the delivery** of siRNA targeting p53 into cancer cell lines. When associated with CADY carrier, sub-nanomolar concentrations of p53 siRNA significantly knocked down p53 protein levels. **Given its biological** properties, we believe that CADY-based technology will contribute significantly to the development of fundamental and therapeutic applications of siRNA