

**P017** Intracellular fate of CPP disulfide-linked PNAs

**Fatima Boutimah-Hamoudi**<sup>1, 2, 3</sup> and

**Tula Ester Saison-Behmoaras**<sup>1, 2, 3</sup>

<sup>1</sup>CNRS, UMR5153, Paris, F-75005, France, <sup>2</sup>Inserm, U565, Paris, F-75005, France, <sup>3</sup>Muséum National d'Histoire Naturelle, USM503, Paris, F-75005, France

Therapeutic potential of antisense peptide nucleic acids (PNAs) has been so far limited by their almost inexistant cellular uptake. Coupling PNAs with the cell penetrating peptide (CPP) cargos seems to be a promising way to enhance their delivery. Several peptides and coupling ways have already been tested but no general guideline emerged about the structural features requirements. Namely, the need of a cleavable disulfide bond or a stable linkage between carrier and cargo hasn't been ascertained. To improve our understanding of conjugate uptake mechanisms we developed a system that allows us to test both biological activity and specificity of PNAs and different combinations of conjugates. These latter targeted a polypurine tract sequence and its mutated counterparts which had been inserted in downstream of a luciferase and GFP reporter gene coding sequence, respectively. To test them straightforward within the cells we used a bacterial permissive agent, Streptolysine-O. In this conditions, we investigate the intracellular fate of the conjugates in biological versus reducing conditons. In particular, we compare their biological activity and their subcellular localization by confocal fluorescent microscopy of unfixed cells. We have already revealed high specificity and activity of two PNAs. These were selected for disulfide coupling with peptides of different chemistries: the well-known penetratin and two new peptides. Preliminary results will be discussed here.