

**P005** Impact of the carrier nature on the cellular uptake efficiency and the intracellular localization  
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Cell-penetrating peptides (CPPs) have been shown to enter cells via different pathways including direct membrane translocation and endocytosis. One of the essential questions that now remain to be clarified concerns the possible existence of elements in the CPP chemical structure that could favour a given route of entry and allow specific intracellular targeting. Using an original library of pseudo-peptidic and peptidic carriers, we have explored the impact on internalization of the nature and spatial distribution of cationic and lipophilic functional groups. Nine new pseudo-peptidic carriers have been synthesized all incorporating in their sequence the  $\alpha,\alpha$  disubstituted amino acid bis-ornithine. This amino acid offers great versatility in the design of polymers with linear or dendritic structure and the grafting of multiple functionalities. We have compared the properties of the various carriers to deliver the same peptidic cargo. Quantification of the internalized cargo and the study of its intracellular degradation were performed by a method based on MALDI-TOF MS. Its intracellular localization was studied by confocal microscopy. Data show that the chemical structure of the carrier can have a strong impact on the intracellular localization.