Alfredo Erazo-Oliveras et al., Pharmaceut Anal Acta 2014, 5:3
http://dx.doi.org/10.4172/2153-2435.S1.021

OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference and Exhibition on
Pharmaceutics & Novel Drug Delivery Systems
March 24-26, 2014 Hilton San Antonio Airport, San Antonio, USA

Cytosolic delivery of proteins and cell-impermeable small molecules into live cells by incubation with an endosomolytic multivalent cell-penetrating peptide derived from TAT

Alfredo Erazo-Oliveras, Kristina Najjar, Laila Dayani, Ting-Yi Wang, Gregory A. Johnson and **Jean-Philippe Pellois**
Texas A&M University, USA

Macromolecular delivery strategies typically utilize the endocytic pathway as a route of cellular entry. However, endosomal entrapment severely limits the efficiency with which macromolecules penetrate the cytosolic space of cells. Herein, we report on how a multivalent cell penetrating peptide derived from the prototypical peptide TAT, mTAT, penetrates live cells by escaping from endosomes with a particularly high efficiency. By mediating endosomal leakage, mTAT also delivers small molecules, peptides, and proteins into cultured cells after a simple co-incubation procedure. Cytosolic delivery is achieved in most cells in a culture, in several mammalian primary cells and cell lines, and only a relatively small amount of material remains trapped inside endosomes. Delivery does not require binding interactions between mTAT and a target cargo, multiple molecules can be delivered at once, and delivery can be repeated. Remarkably, mTAT-mediated delivery does not noticeably impact cell viability, proliferation, or gene expression. mTAT-mediated delivery was evaluated with HoxB4, a transcription factor with therapeutic potential for hematopoietic stem cells expansion *in vitro*. Addition of mTAT to the incubation media augments the induction of a luciferase reporter 24-fold over that obtained for HoxB4 alone and 61-fold over that obtained with TAT-HoxB4, a protein construct fused to TAT. Finally, by changing the stoichiometry of mTAT and HoxB4 administered extracellularly, the transcriptional activity of HoxB4 could be precisely controlled. Overall, this new delivery strategy should be extremely useful for cell-based assays, cellular imaging applications, and the *ex vivo* manipulation and reprogramming of cells.

Biography

Alfredo Erazo-Oliveras completed his B.S. in Chemistry and Environmental Sciences at the age of 22 years from the University of Puerto Rico, Río Piedras Campus. He is currently a graduate student/Ph.D. candidate working in Dr. Jean-Philippe Pellois laboratory at the Department of Biochemistry and Biophysics in Texas A&M University, College Station. He has published 6 papers including one review paper titled "Improving the Endosomal Escape of Cell-Penetrating Peptides and Their Cargos: Strategies and Challenges" which reviews evidence concerning cell-penetrating peptide's endosomolytic activity as well as strategies used to increase cytosolic delivery of CPP-cargoes.

alfredo_erazooliveras@neo.tamu.edu