Title	Novel Polymeric Micelles for siRNA Delivery
Keywords (up to 5)	Cancer, gene therapy, polymeric micelles, siRNA delivery
Authors	Franck MARQUET[1], Gerrit BORCHARD[1] [1]*School of Pharmaceutical Sciences, University of Geneva, University of Lausanne, Switzerland*
Abstract	Gene therapy is considered a promising method for cancer treatment. Despite all optimism that therapeutics based on RNA interference has aroused, there are still some challenges to face for a successful delivery. Regarding non-viral vectors, polymeric micelles constitute a more recent class of nanosystems [1], which might overcome transfection problems of nucleotide-based therapeutics. Complexation of siRNA with biocompatible polycations in a micellar system requires the selection of cationic charge density and the appropriate size of the polymer for an optimum balance between safety and efficacy. Polylysine (PLL, 1.3kDa) was selected based on computational simulation of binding mechanism to a siRNA against human STAT3 [2]. Preparation of amphiphilic co-polymers was performed by coupling PLL with boc protection to polyethylene glycol methyl ether (PEG, 2kDa) by a carbodiimide reaction. This was followed by a polymerization of lactide with PEG-PLL acting as macroinitiator. The primary amines were deprotected successively. Micelles were prepared by an evaporation technique and the mean size determined by dynamic light scattering (DLS) at an angle of 90° at 25°C using a Malvern Zetasizer, and by transmission electron microscopy. Fluorescence measurements were performed using Nile Red to determine the critical micellar concentration (CMC). *In vitro* cytotoxicity assays were performed by WST-1 on lung carcinoma cells (A549) and prostate cancer cells (PC3).
References	1. Shi, J., et al. (2017). "Cancer nanomedicine: progress, challenges and opportunities." Nat Rev Cancer 17(1): 20-37. 2. Grasso, G., et al. (2017) “Free Energy Landscape of siRNA-polycation complexation: Elucidating the effect of molecular geometry, polymer flexibility, and charge neutralization.” PLoS One 12(10): e0186816