15th International Conference on
PHARMACEUTICAL FORMULATIONS & DRUG DELIVERY
September 17-18, 2018 | Philadelphia, USA

Targeted anti-cancer drug delivery system based on aptamer-decorated polymeric nano-vehicles

Shira Engelberg[1], **Yehuda G Assaraf**[2] **a**nd **Yoav D Livney**[1]
[1]Israel Institute of Technology, Israel
[2]Technion-Israel Institute of Technology, Israel

Lung cancer is the leading cause of cancer mortality worldwide, (88% deaths of diagnosed patients). Hence, novel therapeutic modalities are urgently needed. Conventional chemotherapeutic regimens are non-selective, resulting in severe adverse side effects to healthy tissues. Herein we develop a targeted drug delivery system against non-small-cell lung cancer (NSCLC), composed of a biocompatible block-copolymer, PEG-PCL, entrapping the hydrophobic chemotherapeutic drug paclitaxel (PTX) within its micelles. To achieve selective targeting the nanoparticles (NPs) were decorated with single-stranded oligonucleotide-based S15 aptamers (S15-APTs). In a preceding study, we found that S15-APTs decorated NPs enter these cells via clathrin-mediated endocytosis. This entry pathway enables to evade plasma membrane-localized multidrug resistance efflux pumps, thereby overcoming an important mechanism of cancer multidrug resistance (MDR). PEG-PCL/PTX NPs where prepared by surfactant-free nanoprecipitation. To form NPs that will be able to undergo endocytosis, we aimed at forming NPs <50 nm. The critical micelle concentrations (CMC) was determined to be 5 μM. The drug loading capacity (LC) and encapsulation efficiency (EE) were determined by HPLC with increasing drug to polymer ratios. The optimized formulation was 1:0.4 molar ratio of PEG-PCL: PTX with EE=77±13% and LC=47±8 (ug PTX/ mg PEG-PCL). To examine system stability, the average size and ζ-potential were measured after 24 hours. NPs functionalized with S15-APT displayed an average size of 44±2 nm, whereas the NPs without S15-APTs aggregated to micron-sized particles. This is due to charge repulsion of the highly negatively charged SSDNA APTs. Hence, the APTs are not only a targeting moiety but also a colloidally-stabilizing element and their addition counterintuitively reduces NP size, which is crucial for entrance into the target cells. These results were further supported by ζ-potential measurements demonstrating almost two folds increase in negative ζ-potential in the APT-decorated system as opposed to non-decorated NPs (-24.4 and -13.7 respectively).

Biography

Shira Engelberg received her BSc in Biotechnology and Food Engineering from the Technion-Israel Institute of Technology (2016). She joined Prof. Livney's group in September 2015. Her research is done under the co-supervision of Professor Yoav D Livney and Professor Yehuda G Assaraf. Her previous project was enhancing the bioavailability of insoluble bioactive. In her PhD, she is focusing on developing a novel targeted anti-cancer drug delivery systems based on aptamer-decorated polymeric nano-vehicles and has published a paper studying the specificity of S15-aptamers to target A549 cells and the mechanism of entry into the target cells.

shiraengelberg1@gmail.com

Notes: