Nucleic acids are promising drug candidates as they can address diseases with few druggable targets. Nevertheless, nucleic acids are challenging to deliver because of their unfavorable physicochemical properties and poor stability in biological fluids. Lipid nanoparticles (LNPs) have been the mainstay of nucleic acid carriers; however, LNPs show ~80-90% accumulation in the liver after systemic administration and are hence indicated only for hepatic or local delivery applications. Therefore, we developed Nanosac, a deformable and biocompatible polydopamine nanocarrier, to enable systemic delivery of siRNA to solid tumors. This seminar discusses the optimization, *in vitro* characterization, and *in vivo* testing of Nanosac ability to deliver siRNA to silence two immune checkpoints in tumor-bearing mouse models. Further, it discusses the Nanosac potential to improve tolerability of the anticancer drug carfilzomib by reducing its accumulation in the blood-filtering reticuloendothelial system (RES).