A Tumor-on-a-Chip Strategy to Examine the Impact of the Design of Lipid Nanoparticles on their Transportation into 3D Ovarian Tumor

Armin Tahmasbi Rad 1,2, Wafa Aresh, Ph.D. 1, Mu-Ping Nieh, Ph.D. 1,2,3

1 Biomedical Engineering Department, University of Connecticut, Storrs, CT
2 Institute of Materials Science, Polymer Program, University of Connecticut, Storrs, CT
3 Chemical and Biomolecular Engineering Department, University of Connecticut, Storrs, CT

The usage of nanoscale materials for cancer therapeutics and diagnostics is growing rapidly. However, there remain many challenges to understand the controlling parameters (e.g., optimum size, shape, chemical properties) that significantly affect the performance of the nano-bio interactions due to complicated in vivo environments. It has been shown that conventional 2D cell cultures affect cancer cell behavior and in absence extracellular matrix they might not be representative for the in vivo study. In this work, we developed a 3D tumor cultured in a microfluidic chamber made of polydimethylsiloxane (PDMS) which can mimic the tumor environment. The developed model was then used in order to understand our universal discoidal bicelle platform which is capable to encapsulate a wide range of diagnostic and therapeutic molecules/clusters. The nanoparticle penetration and transport in ovarian cancer cell–gel cultures were studied and compared to current commercialized clinical carriers. The ovarian human cancer cells (OVCAR-8) were embedded in 4-arm Poly(ethylene glycol) acrylate hydrogel which was loaded in the chamber, mimicking the extracellular matrix around the tumors. The microfluidic device can be rapidly fabricated offering direct in vitro cell imaging. The designed protocol can be configured easily allowing controllable microenvironment for different cell lines. To combine the NP study with the application of the microfluidic device, the transportation of two shape-distinct fluorescently labeled lipid self-assembly nanoparticles were investigated. The result indicates that the penetration of nanoparticles can be significantly enhanced by differentiating the shape of them as well as by using active targeting molecules such as Folate.

Figure 1. a) The diameter of the grown ovarian tumors in the microfluidic device during a 15-day period. b) The effect of NPs shape and active targeting molecule on tumor accumulation. The quantification of fluorescently labeled discs and vesicles penetration into the tumor tissue during the first hour. c) Comparison of active and passive accumulation in tumor tissue after 12 hours. Scale bar is 100 µm.