Geometry Matters: Cellular Uptake of Nanoscale Drug Carriers is Uniquely Dependent on Particle Size and Shape

Rachit Agarwal, Vikramjit Singh, Patrick Jurney, Li Shi, SV Sreenivasan, Krishnendu Roy.
Biomedical Engineering, Mechanical Engineering, University of Texas at Austin

Statement of Purpose: Shape-specific Nanoparticles, inspired by the diverse evolutionary conserved shapes of pathogens and cells found in nature, are gaining significant interest as carriers to efficiently deliver payload across biological barriers. Our group has recently developed unique nanoimprint-based techniques to fabricate, biocompatible polymeric drug nanocarriers of precise sizes and shapes that can release drugs primarily in the presence of specific environmental signals, e.g. enzymes.(*1-3*) The objective of this study was to study the effects of nanoparticle size and shape on uptake in both epithelial and endothelial cells.

Methods: Nanoimprinting was performed to form precise shaped polyethylene glycol diacrylate (PEGDA) particles using the IMPRIO 100 Jet and Flash Imprint Lithography (J-FIL) system (Molecular Imprints, Austin, TX) and the formed particles were characterized using the techniques previously described.(3) Cellular uptake of nanoparticles was evaluated using confocal microscopy and flow cytometry. Pharmacological inhibitors were used to study the different uptake pathways involved for different shapes.

Results and Discussion: Using J-FIL, particles of 5 different geometry were successfully imprinted with feature dimensions as (Cuboids (all dimensions in nm): 800x100x100, 400x100x100 and Cylinders (diameter in nm x height in nm): 350x100, 240x100, 100x60). Cellular uptake was quantified using flow cytometry with all 5 shapes of nanocarriers in HEK293, HeLa and HUVEC cells. It was found that disc shaped particles were more efficiently uptaken than rod shaped particles of similar volume in all cell lines. Further larger volume discs and rods were able to deliver more median fluorescence as compared to smaller volume discs and rods respectively in epithelial cell lines while endothelial cells has an optimal size and shape at which maximal uptake is achieved. It was found that discs and rods employ different uptake pathways accounting for this difference in uptake efficiencies

Conclusion: We have shown our ability to fabricate monodisperse and biocompatible polymeric nanoparticles of precise shape and size. Uptake studies have shown that geometry matter and that different cell lines responds differently to shape-specific particles. This difference in internalization efficiency is due to difference in uptake mechanisms that is triggered based on geometry of the particles and cell lines used. This understanding of the effect of shape on cellular uptake allows us to better design of nanocarriers for efficient delivery of biological payload to target cells.

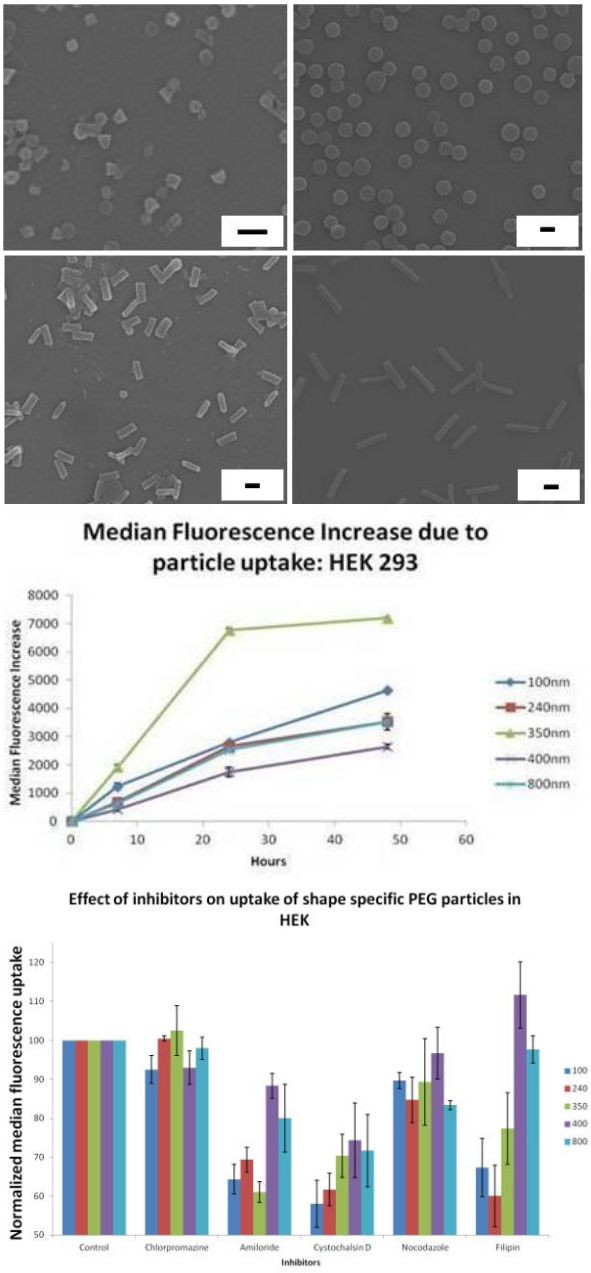

Figure 1: (a) SEM micrographs of 100x60nm cylindrical particles, 350x100nm cylindrical particles, 400x100x100nm cuboidal particles, 800x100x100nm cuboidal particles, (b) Median Fluorescence increase due to particle uptake in HEK 293 cells, (c) Relative change in uptake due to blocking different pathways using pharmacological inhibitors.

References:

1. Glanchai LC *et al. J. Control Release* 2008, 125 (3), 263.
2. Caldorera-Moore M *et al. Soft Matter* 2011, 7, 2879.
3. Agarwal R *et al. ACS Nano* 2012, 6, 2524

©2013 Society For Biomaterials