

Physics-Inspired Micro/Nanotherapeutics: Same Problem, Different Approaches

Significance of physical aspects of *in vivo* microenvironment relevant to transport and action of therapeutics has begun to be recognized. For example, pathophysiological characteristics of the tumor microenvironment result in poor delivery of drug molecules to targeted cancer cells. These characteristics include irregular and nonfunctional vasculature, dense extracellular matrix, high cell packing density, and an elevated interstitial fluid pressure. In addition, cellular drug resistance also appears to be mediated by integrin signaling associated with adhesion of cancer cells to the extracellular matrix. These emergent properties of the complex tumor microenvironment result in spatiotemporally heterogeneous and transient cellular responses to drugs, posing significant challenges to effective treatment. In order to design innovative and effective therapeutics to overcome these complex barriers, thus, highly interdisciplinary collaborative approaches are crucial to design, synthesize, and characterize.

This special issue was originated when I was cochairing the track “Nanotherapeutics” of ASME (American Society of Mechanical Engineers) 2015 NanoEngineering for Medicine and Biology Conference with Professor Carston Wagner from the University of Minnesota. While we were planning the track, we found that there are clear needs for a venue to exchange ideas from different disciplines and disseminate challenges to develop new and innovative therapeutics. This issue aims to showcase and discuss recent interdisciplinary approaches, particularly based on physics principles, on design, development, and characterization of micro- and nanotherapeutics. In a perspective paper,¹ Dr. Kinam Park suggests a need of paradigm change of invention cycle for a drug delivery system, which will need highly active interdisciplinary collaboration based on clear definition and recognition of the pressing problems of developing drug and drug delivery systems. He also shares his thoughts about how to facilitate collaborations from the perspectives of researchers, funding agencies, and academicians.

In addition, research papers were invited to highlight state-of-the-art approaches of physics-inspired micro/nanotherapeutics. Schmidt et al.² present a way to amplify the effects of vascular endothelial growth factor and stimulate endothelial cells' morphogenesis by use of chemically modified alginates, and demonstrate that the modification can increase sprouting of endothelial cells. In the study, the binding kinetics of the growth factor is intervened by alginates modified with a controlled number of sulfate groups. Modulation of drug delivery systems' physical characteristics—size, surface charge, and shape—is also presented.³ Therapeutic systems to deliver energy to create localized heating for cancer therapy are proposed.⁴ Shah et al.⁵ report the evaluation of chemically self-assembled nanorings, which show great potential to be used as a platform targeting various receptors and molecules. In their *in vivo* evaluation, multiple transport characteristics are evaluated including circulation, extravasation, and binding kinetics. Development of *in vitro* tumor models and their use to assess

the cellular pharmacokinetics of a drug and drug delivery system are also demonstrated.⁶ Last, but not least, a new and emerging physical view on multicellular chemical sensing and drug response is reviewed by Varennes and Mugler.⁷

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Notes

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Special Issue: Physics-Inspired Micro/Nanotherapeutics

Published: July 5, 2016

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