Guiding Principles of Nanoparticle Uptake by Biological Cells

Dr. sulin Zhang, Mr. Hongyan Yuan, Dr. Ju Li, Dr. George Lykotrafitis, Dr. Gang Bao & Dr. Subra Suresh

Tumor-specific drug delivery has long been desired in chemotherapeutic cancer treatment for achieving enhanced therapeutic efficacy and for mitigating adverse side effects. Most existing anticancer agents are incapable of distinguishing between benign and malignant cells, and consequently they cause systematic toxicity during chemotherapy. Owing to their small size, ligand-coated NPs can be efficiently directed toward, and subsequently endocytosed by tumor cells through ligand-receptor recognition and interaction, thereby offering an effective approach for specific targeting of tumor cells. In the present work, we present a thermodynamic model for receptor-mediated endocytosis of ligand-coated NPs. The model reveals that cellular uptake of NPs is interrelatedly dependent on the particle size and ligand density, and the dependence can be characterized by a two-dimensional phase-diagram. Meeting at a triple point, the lower and upper phase transition boundaries encompass a region in which the cellular uptake is appreciably larger than other regions. An optimal condition for maximized cellular uptake is identified. We rationalize the biophysical mechanisms governing the phase transition boundaries based on energetics and entropics. Our model predictions agree with a set of prior experimental data in several aspects, including the size dependence and the maximal uptake. The model also motivates new, well controlled experiments to further explore the interrelated effects. The constructed phase-diagram of NP endocytosis provides valuable guidance to the rational design of NPs for cell-specific targeting, which may find a wide range of biomedical applications in bioimaging, biotracking, biosensing, and anticancer drug delivery.

Topic(s): Biomechanics ; Symposia: Interfacing Bio and Nano Phenomena (Tian Tang, Yaling Liu, and Wei Hong)

Date submitted: Mar 31, 2009