Polymeric nanoparticles have wide application in varied fields including drug delivery and medical imaging. Particle’s properties have significant impact on their performance including circulation half-life, drug release rates and toxicity. Our research aims at developing quantitative guidelines describing the relationships between nanoparticle design and their performance as a drug delivery carrier. We particularly focus on engineering particle shape, a design parameter that has received little attention in the past. We have devised methods to generate particles of several distinct shapes and studied their impact on key processes in drug delivery including phagocytosis, circulation, adhesion of vascular walls, and targeting. Based on this understanding, we have designed novel polymeric particles that demonstrate reduced phagocytosis and enhanced targeting. Our studies demonstrate that particle shape provides a new dimension in engineering of polymeric carriers and opens up new opportunities in drug delivery. In addition to shape, we demonstrate that controlling mechanical properties of carriers also offers unique opportunities. Specifically, we have synthesized flexible particles made from proteins that mimic the physical and functional properties of body’s own circulating cells such as red blood cells. Particles that mimic the size, shape and flexibility of natural circulating cells offer advantages that are typically lacking in standard spherical polymeric particles. The motivation to use physical properties of nanoparticles to control biological function is provided by the biology itself. In nature, numerous examples can be found where physical aspects, such as shape, mechanical properties and compartmentalization are crucial to biological function. We demonstrate that physical attributes such as size, shape and mechanical properties form essential building blocks of biology. This revelation forms the basis of the new paradigm in design of nanoparticles.