Nanoscience and Biology:
Connecting Nano to Micro and Milli for In Vitro Interrogation and Control

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Nanoscience provides biology and medicine with a remarkably powerful set of tools for interrogating and controlling living systems. In vivo, nanoparticles can deliver drugs that target specific organs or cells and provide readouts of microenvironmental conditions. Nanostructures can serve as scaffolds that create particular conditions that, for example, enhance tissue growth or repair. In vitro, nanoparticles can serve the same functions and in addition offer the possibility of closed-loop control of biological systems. Nanofabricated substrates can provide particular cellular microenvironments or barriers. Such applications are particularly important in organ-on-chip (OoC) studies that are designed to recapitulate human physiology, pathology, and toxicology, albeit on the milli- to micro-scales yet with realistic organ-organ interactions. Several challenges confront OoC experiments: a realistic microhuman OoC system, termed a microhomunculus, will have a total cell mass of less than 70 mg, and a “blood” volume of about five microliters. Nanoscience may be critical in providing rapid, low-cost, multiplexed readouts of the physiological state of coupled individual organs in the system. The readouts need to either be non-destructive and non-toxic, or require withdrawal of no more than a microliter of fluid a day for testing, suggesting, for example, very low volume, high sensitivity, multiplexed, bar-coded affinity microbead assays. The readout device also needs to be compact and low-cost, so that large numbers of the systems can be used in parallel for drug development or toxicology. Hence the nano-to-milli interface challenge. Given appropriate readouts, it is then possible to control the system – either through injection of regulatory hormones, nutrients and growth factors into the circulation, or the optical or chemical release of caged regulatory compounds. Optical control of the activity of multiple classes of nanoparticles would be an ideal solution to the milli-to-nano interface challenge. Such bidirectional interfaces between the laboratory and sub-cellular spatial scales should advance not only drug development and toxicology, but also our understanding of physiology and systems biology.