NANOBIOTECHNOLOGY

FOR DRUG DELIVERY AND TISSUE ENGINEERING

Ali Khademhosseini,
Robert Langer
Massachusetts Institute of Technology

Nanotechnology is an emerging field that could potentially make a major impact to human health. Nanomaterials promise to revolutionize medicine and are increasingly used in drug delivery or tissue engineering applications.

Nanotechnology has become a rapidly growing field with potential applications ranging from electronics to cosmetics. Richard Feynman, introduced the concept of nanotechnology in his pioneering lecture "There's plenty of room at the bottom" at the 1959 meeting of the American Physical Society. However, only recently has our ability to harness the properties of atoms, molecules and macromolecules advanced to a level that can be used to build materials, devices and systems at the nanoscale.

The term "nanotechnology" varies greatly based on the specific definition that is used. National Science Foundation and the National Nanotechnology Initiative define nanotechnology as understanding and control of matter at dimensions of 1-100 nm where unique phenomena enable novel applications. In this manuscript, we use a similar definition, however, we also discuss molecular structures, materials and devices with dimension of 1-100 nm in one of their dimensions. Thus, incorporating miniaturization approaches that generate nanofabricated structures such as nanopatterns and nanotextures. Interestingly, much of what we know about bulk properties of materials breaks down at these length scales. For example, nanomaterials such as carbon nanotubes and gold nanoparticles have physical properties that are different than their bulk counterparts. Therefore, such technologies generate new opportunities and applications.

Nanoscale materials and devices can be fabricated using either 'bottom-up' or 'top-down' fabrication approaches. In bottom-up methods, nanomaterials or structures are fabricated from buildup of atoms or molecules in a controlled manner that is regulated by thermodynamic means such as self-assembly (*1*). Alternatively, advances in microtechnologies can be used to fabricate nanoscale structures and devices. These techniques, which are collectively referred to as top-down nanofabrication technologies, include photolithography, nanomolding, dip-pen lithography and nanofluidics (*2, 3*). It is perhaps because of the breadth of different approaches in the synthesis and fabrication nano-molecules and nano-devices that chemical engineers are playing a key role in advancing the field of nanotechnology. On one hand, chemical engineers possess the ability to understand molecular events through modeling and simulation as well as thermodynamic and kinetic calculations, while on the other hand, they have the ability to understand systems, device miniaturatizaion and fluidics associated with top-down fabrication strategies.

Nanomaterials and devices provide unique opportunities to advance medicine. The application of nanotechnology to medicine is referred to as "nanomedicine" or "nanobiomedicine" and could impact diagnosis, monitoring, and treatment of diseases as well as control and understanding of biological systems. In this review, we discuss the use of nanotechnology for medical applications with focus on its use for drug delivery and tissue engineering. Specifically, we discuss bottom-up and top-down nanofabrication technologies and their use in various drug delivery and tissue engineering applications.

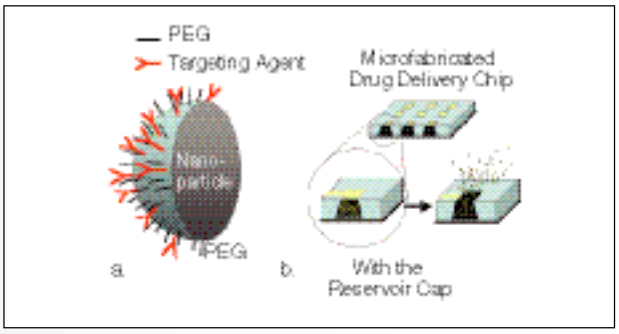
Nanotechnology for drug delivery

Controlled drug-delivery strategies have made a dramatic impact in medicine. In general, controlled-release polymer systems deliver drugs in the optimum dosage for long periods, thus increasing the efficacy of the drug, maximizing patient compliance and enhancing the ability to use highly toxic, poorly soluble or relatively unstable drugs. Nanoscale materials can be used as drug delivery vehicles to develop highly selective and effective therapeutic and diagnostic modalities (*4–6*). There are a number of advantages with nanoparticles in comparison to microparticles. For example, nanoscale parti-

cles can travel through the blood stream without sedimentation or blockage of the microvasculature. Small nanoparticles can circulate in the body and penetrate tissues such as tumors. In addition, nanoparticles can be taken up by the cells through natural means such as endocytosis. Nanoparticles have already been used to deliver drugs to target sites for cancer therapeutics (*7*) or deliver imaging agents for cancer diagnostics (*8*). These vehicles can be engineered to recognize biophysical characteristics that are unique to the target cells and therefore minimize drug loss and toxicity associated with delivery to non-desired tissues.

In general, targeted nanoparticles comprise of the drug, the encapsulating material and the surface coating (Figure 1a). The encapsulating material could be made from biodegradable polymers, dendrimers (treelike macromolecules with branching tendrils that reach out from a central core) or liposomes (spherical lipid bilayers). Controlled release of drugs (such as small molecules, DNA, RNA or proteins) from the encapsulating material is achieved by the release of encapsulated drugs through surface or bulk erosion, diffusion, or triggered by the external environment, such as changes in pH, light, temperature or by the presence of analytes such as glucose (*6*). Controlled-release biodegradable nanoparticles can be made from a wide variety of polymers including, poly (lactic acid) (PLA), poly (glycolic acid) (PGA), poly (lactic co-glycolic acid) (PLGA) and polyanhydride. PGA, PLA and their co-polymer PLGA are common biocompatible polymers that are used for making nanoparticles. Since PGA is more susceptible to hydrolysis than PLA, by changing the ratio of these two components, PLGA polymers can be synthesized with various degradation rates. Current research into novel nanomaterials is aimed at improving the properties of the materials such as biocompabitility, degradation rate and control over the size and homogeneity of the resulting nanoparticles.

In order to control the targeted drug delivery of intravenously delivered nanoparticles, nanoparticle interactions with other cells such as macrophages must be controlled. Various approaches have been developed to control these interactions ranging from changing the size of the particle to changing nanoparticle surface properties. To remove nonspecific protein adhesion and decrease uptake by macrophages, nanoparticles can be functionalized using protein replant materials such as poly(ethylene glycol) (PEG) (*7*) and polysaccharides (*8*, *9*). Nonadhesive surface coatings increase the circulation time of the nanoparticles (*7*) and reduce toxic effects associated with non-targeted delivery (*10*, *11*). More recently, novel approaches aimed at conjugating small molecules on nanoparticles using high-throughput methods have yielded nanoparticle libraries that could be subsequently



■ Figure 1. Schematic diagram of examples of bottom-up and top-down nanotechnology approaches for controlled drug delivery: (a) shows an illustration of a controlled-release nanoparticle cut-in half. The nanoparticle may contain drugs and will be coated with PEG molecules and targeting molecules to regulate its interactions inside the body; (b) shows a microfabricated drug-delivery device containing reservoirs that contain drugs. As the cap for each reservoir is removed the drug will be released.

analyzed for their targeted properties (*12*). Also, noncovalent approaches have been used to surface modify nanoparticles. For example, the layer-by-layer deposition of ionic polymers have been used to change surface properties of nanoparticles, such as quantum dots (*13*). Layer-by-layer methods alter the surface charge of nanoparticles, which has been shown to regulate nanoparticle biodistribution. For example, increasing the charge of cationic pegylated liposomes decreases their accumulation in the spleen and blood, while increasing their uptake by the liver and tumor vessels (*14*).

To eliminate the need for surface modification schemes, amphiphilic polymers may be synthesized by covalently linking biodegradable polymers to PEG prior to formation of nanoparticles. For example, nanoparticles can be synthesized from amphiphilic copolymers composed of lipophilic (*i.e.*, PLGA or PLA) and hydrophilic (*i.e.*, PEG) polymers. Upon formation of these nanoparticles, PEG migrates to the surface in the presence of an aqueous solution forming pegylated nanoparticles (*7*).

To target nanoparticles to the desired tissues, a number of methods have been developed. These include physical means such as controlling the size, charge and hydrophobicity of the particles. In addition, targeting molecules, such as antibodies and peptides, that recognize specific cell surface proteins and receptors, can be conjugated to the nanoparticle surface to specifically target specific cell types. Antibodies and peptides have been successfully used to target nanoparticles to a number of desired cell types and provide powerful means of directing controlled-release nanoparticles to specific sites in the body. Potential disadvantages of antibody- and peptide-based targeting include their batch-to-batch variation and their potential immunogenecity. Aptamers, a class of DNA- or RNA-based ligands, may overcome some of the limitations associated with antibody- and

peptide-based drug delivery. Aptamers have been conjugated to nanoparticles to generate nanoparticles that can target prostate cancer cells (*15*, *16*).

Current research in targeting the delivery of nanoparticles involves validating the *in vivo* efficacy of the various targeting approaches and developing methods of enhancing the targeting of the particles without side effects. Future generations of nanoparticles promise to not only deliver drugs to the desired sites within the body, but also in a temporally regulated manner. For example, nanoparticles have recently been generated that can be used to sequentially deliver drugs to cancer cells so that each drug is delivered at the proper time to induce cell death as well as prevent angiogenesis (*17*). It is envisioned that the development of "smart" nanoparticles could be a powerful means of further enhancing the functionality of these nanoparticles.

In addition to polymeric nanoparticles, other types of nanomaterials have also been used for medical applications. For example, quantum dots, nanoparticles with novel electroluminescent properties and magnetic resonance imaging (MRI) contrast agents have been used to image cancer cells. Also, carbon nanotubes and nanowires and nanoshells have also been used for various therapeutic and diagnostic applications (*18*). Each of these materials provides unique physical, chemical and biological properties that are based on the nanoscale size and structure of the materials. For example, quantum dots are more stable than chemical fluorphores, have tighter emission wavelengths and can be engineered to emit at specific wavelengths by changing its size. Thus, the targeted delivery of these materials could potentially lead to significant medical breakthroughs.

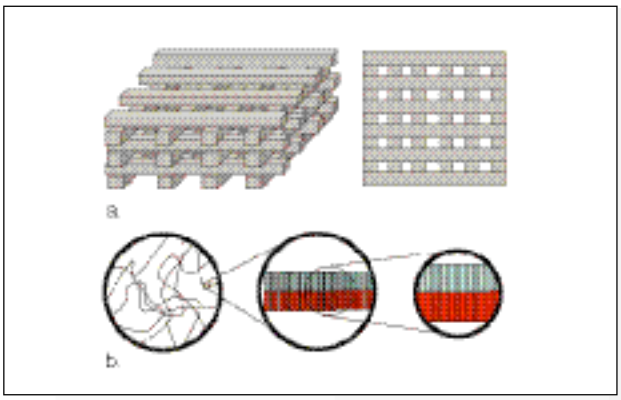
Top-down nanofabrication and microfabrication approaches based on integrated circuit processing may be used to fabricate controlled-release drug delivery devices. Using photolithographic and integrated circuit processing methods, silicon-based microchips have been fabricated that can release single or multiple chemicals on demand using electrical stimuli (*19*) (Figure 1b). These engineered microdevices can be used to maintain biological activity of the drugs and facilitate the local, accurate, controlled release of potentially complex drug-release profiles. In addition to silicon-based devices, polymeric-based microfabricated devices have been made that can release drugs based on the degradation of polymeric reservoir covers (*20*). Microfabrication techniques have also been used to develop transdermal drug delivery approaches based on microneedles (*21*). These microfabricated needles, which are much smaller than hypodermic needles, may be used to deliver drugs in a painless and efficient manner. By penetrating through the outer 10–20 μm of skin, microneedles can deliver drugs without activating sensory nerves of the tissue, thus providing a painless method of delivering drugs. Although the above examples have been performed using microscale resolution, the current state-of-the-art in top-down nanofabrication approaches can generate features that are less than 100 nm in resolution. Therefore, the fabrication of nanoscale devices using these approaches is theoretically possible and may be advantageous for specific drug-delivery applications in which miniaturized nanoscale devices are desired.

Interestingly, bottom-up and top-down approaches have merged to optimize drug-delivery vehicles. For example, microfabricated approaches have been used to develop microfluidic devices that mimic the body's vasculature and can be used to test and optimize the interaction of targeted nanoparticles with the cells that line the cancer blood vessels (*15*). By changing parameters such as shear stress and geometry of the channel, as well as nanoparticle properties such as size, and surface properties optimized nanoparticle formulations can be obtained before performing costly animal and clinical experiments.

Nanotechnology in tissue engineering

Tissue engineering combines biology, medicine, engineering and materials science to develop tissues that restore, maintain or enhance tissue function (*22*). To recapitulate proper function and organization of real tissues in tissue engineering approaches, it is important to mimic tissue properties at the nanoscale. For example, in the body, the extracellular matrix (ECM) provides a natural web of tissue-specific and organized nanofibers that support and maintain the cell microenvironment. In addition, cells in the body reside in a unique environment that is regulated by cell-cell, cell-ECM and cell-soluble factors presented in a spatially and temporally dependent manner. Thus, engineering approaches and methods that aim to be use tissue engineering principles must have the same level of complexity. Nanotechnologies and microtechnologies can be merged with biomaterials to generate scaffolds for tissue engineering that can maintain and regulate cell behavior. Also, such technologies can be used to regulate *in vitro* cellular microenvironment to direct stem cell differentiation (Figure 2).

Many tissue engineering approaches rely on the use of 3D biodegradable scaffolds that place cells in close proximity to each other. Inside these scaffolds, cells deposit their own matrix and as the scaffold degrades, they form a 3D tissue structure that mimics the body's natural tissues. Nanofabricated and microfabricated tissue engineering scaffolds have the potential to direct cell fate as well as regulate processes such as angiogenesis and cell migration. Both top-down and bottom-up technologies have been used to incorporate nanoscale control for tis-



■ Figure 2. Schematic diagram of the bottom-up and top-down nanotechnology approaches for tissue engineering: (a) Nanofabrication approaches can be used to generate 3D tissue engineering scaffolds with controlled pore geometries, shapes and degradation properties; (b) In addition, nanotechnology can be used to generate tissue engineering scaffolds from self-assembly of nanomaterials such as amphiphilic peptides that generate higher order structures such as nanofibers.

sue engineering scaffolds. Top-down approaches, such as soft lithography, have greatly enhanced our ability to generate microscale and nanoscale features since they limit the use of expensive clean rooms (*23*).

These approaches have been used for fabricating tissue engineering scaffolds with control over features such as pore geometry, size, distribution and spatial geometry. For example, microfabricated approaches have been used to directly engineer the microvasculature within tissue engineering scaffolds by micromolding biocompatible polymers such as poly(lactide-co-glycolide) (PLGA) and poly(glyceride sebacate) (PGS) (*24–26*). In this approach, a network of microfluidic channels that mimic the tissue microvasculature are fabricated from PLGA or PGS. By stacking multiple layers of these microfabricated plates, tissue engineered scaffolds can be fabricated with nanoscale control. Other approaches such as layer-by-layer deposition of cells and proteins using microfluidic

Literature Cited

1. **Ferrari, M.,** "Cancer Nanotechnology: Opportunities and Challenges," *Nat Rev Cancer,* **5** (3), pp. 161–171 (2005).
2. **Peppas, N. A.,** "Intelligent Therapeutics: Biomimetic Systems and Nanotechnology in Drug Delivery," *Advanced Drug Delivery Reviews,* **56** (11), pp. 1529–1531 (2004).
3. **Sahoo, S. K., and V. Labhasetwar,** "Nanotech Approaches to Drug Delivery and Imaging," *Drug Discov Today,* **8** (24), pp. 1112–1120 (2003).
4. **McCarthy, J. R., *et al.,*** "Polymeric Nanoparticle Preparation that Eradicates Tumors," *Nano Lett,* **5** (12), pp. 2552–2556 (2005).
5. **Gao, X., *et al.,*** "In Vivo Cancer Targeting and Imaging with Semiconductor Quantum Dots," *Nat Biotechnol,* **22** (8), pp. 969–976 (2004).
6. **Langer, R., and D. A. Tirrell,** "Designing Materials for Biology and Medicine," *Nature,* **428** (6982), pp. 487–492 (2004).
7. **G ref, R., *et al.,*** "Biodegradable Long-circulating Polymeric Nanospheres," *Science,* **263** (5153), pp. 1600–1603 (1994).
8. **Lemarchand, C., *et al.,*** "Polysaccharide-decorated Nanoparticles," *Eur J Pharm Biopharm,* **58** (2), pp. 327–341 (2004).
9. **Lemarchand, C., *et al.,*** "Influence of Polysaccharide Coating on the Interactions of Nanoparticles with Biological Systems," *Biomaterials* **27** (1), pp. 108–118 (2006).
10. **Gibaud, S., *et al.,*** "Increased Bone Marrow Toxicity of Doxorubicin Bound to Nanoparticles," *Eur J Cancer,* **30A** (6), pp. 820–826 (1994).
11. **Demoy, M., *et al.,*** "Splenic Trapping of Nanoparticles: Complementary Approaches for In Situ Studies," *Pharm Res,* **14** (4), pp. 463–468 (1997).
12. **Weissleder, R., *et al.,*** "Cell-specific Targeting of Nanoparticles by Multivalent Attachment of Small Molecules," *Nat Biotechnol,* **23** (11), pp. 1418–1423 (2005).
13. **Jaffar, S., *et al.,*** "Layer-by-layer Surface Modification and Patterned Electrodeposition of Quantum Dots," *Nano Letters,* **4** (8), pp. 1421–1425 (2004).
14. **Campbell, R. B., *et al.,*** "Cationic Charge Determines the Distribution of Liposomes Between the Vascular and Extravascular Compartments of Tumors," *Cancer Res,* **62** (23), pp. 6831–6836 (2002).
15. **Farokhzad, O. C., *et al.,*** "Nanoparticle-aptamer Bioconjugates: A New Approach for Targeting Prostate Cancer Cells," *Cancer Res,* **64** (21), pp. 7668–7672 (2004).
16. **Farokhzad, O. C., *et al.,*** "Microfluidic System for Studying the Interaction of Nanoparticles and Microparticles with Cells," *Anal Chem,* **77** (17), pp. 5453–5459 (2005).
17. **Sengupta, S., *et al.,*** "Temporal Targeting of Tumour Cells and Neovasculature with a Nanoscale Delivery System," *Nature,* **436** (7050), pp. 568–572 (2005).
18. **Loo, C., *et al.,*** "Immunotargeted Nanoshells for Integrated Cancer Imaging and Therapy," *Nano Lett,* **5** (4), pp. 709–711 (2005).
19. **Santini, J. T., Jr., *et al.,*** "A Controlled-release Microchip," *Nature,* **397** (6717), pp. 335–338 (1999).
20. **Richards Grayson, A. C., *et al.,*** "Multi-pulse Drug Delivery from a Resorbable Polymeric Microchip Device," *Nat Mater,* **2** (11), pp. 767–772 (2003).
21. **McAllister, D. V., *et al.,*** "Microfabricated Microneedles for Gene and Drug Delivery," *Annu Rev Biomed Eng,* **2,** pp. 289–313 (2000).
22. **Langer, R., and J. P. Vacanti,** "Tissue Engineering," *Science,* **260** (5110), pp. 920–926 (1993).
23. **Whitesides, G. M., *et al.,*** "Soft Lithography in Biology and Biochemistry," *Annual Review of Biomedical Engineering,* **3,** pp. 335–373 (2001).
24. **Borenstein, J. T., *et al.,*** "Microfabrication Technology for Vascularized Tissue Engineering," *Biomedical Microdevices,* **4** (3), pp. 167–175 (2002).
25. **King, K., *et al.,*** "Biodegradable Microfluidics," *Advanced Materials,* **16** (22), pp. 2007+ (2004).
26. **Fidkowski, C., *et al.,*** "Endothelialized Microvasculature Based on a Biodegradable Elastomer," *Tissue Eng,* **11** (1-2), pp. 302–309 (2005).
27. **Tan, W., and T. A. Desai,** "Layer-by-layer Microfluidics for Biomimetic Three-dimensional Structures," *Biomaterials,* **25** (7-8), pp. 1355–1364 (2004).
28. **Vozzi, G., *et al.,*** "Fabrication of PLGA Scaffolds Using Soft Lithography and Microsyringe Deposition," *Biomaterials,* **24** (14), pp. 2533–2540 (2003).
29. **Burdick, J. A., *et al.,*** "Fabrication of Gradient Hydrogels Using a Microfluidics/Photopolymerization Process," *Langmuir,* **20** (13), pp. 5153–5156 (2004).
30. **Zhang, S.,** "Fabrication of Novel Biomaterials Through Molecular Self-Assembly," *Nat Biotechnol,* **21** (10), pp. 1171–1178 (2003).
31. **Silva, G. A., *et al.,*** "Selective Differentiation of Neural Progenitor Cells by High-epitope Density Nanofibers," *Science,* **303** (5662), pp. 1352–1355 (2004).
32. **Deutsch, J., *et al.,*** "Fabrication of Microtextured Membranes for Cardiac Myocyte Attachment and Orientation," *J Biomed Mater Res,* **53** (3), pp. 267–275 (2000).
33. **Thakar, R. G., *et al.,*** "Regulation of Vascular Smooth Muscle Cells by Micropatterning," *Biochem Biophys Res Commun,* **307** (4), pp. 883–890 (2003).
34. **Miller, D. C., *et al.,*** "Endothelial and Vascular Smooth Muscle Cell Function on Poly(lactic-co-glycolic acid) with Nano-structured Surface Features," *Biomaterials,* **25** (1), pp. 53–61 (2004).
35. **Thapa, A., *et al.,*** "Polymers with Nano-dimensional Surface Features Enhance Bladder Smooth Muscle Cell Adhesion," *J Biomed Mater Res A,* **67** (4), pp. 1374–1383 (2003).
36. **Chen, C. S., *et al.,*** "Geometric Control of Cell Life and Death," *Science,* **276** (5317), pp. 1425–1428 (1997).
37. **McBeath, R., *et al.,*** "Cell Shape, Cytoskeletal Tension, and RhoA Regulate Stem Cell Lineage Commitment," *Dev Cell,* **6** (4), pp. 483–495 (2004).

channels (27), microsyringe deposition of PLGA polymer (*28*), photopolymerization within microfluidic channels (*29*) have been used to generate 3D structures with controlled geometries and properties (Figure 2a). The miniaturization of these technologies can be performed to generate scaffolds with sub-100 nm features such as grooves, pores and surface patterns.

Bottom-up approaches based on molecular self-assembly of small building blocks have also been used to generate tissue engineering scaffolds. Research into self-assembly of amphiphilic peptides has shown that they can self-assemble to form hydrogels for tissue engineering (*30*). Self assembled scaffolds can be easily functionalized by incorporating peptide sequences that direct cell behavior directly into the buildup molecule. For example, self assembled gels were fabricated that directed neural stem cell differentiation to neurons and repressed astrocyte differentiation without exogenous growth factors (*31*). These gels were made from peptides that expressed isoleucine-lysinevaline-alanine-valine (IKVAV, an amino acid sequence found in laminin) and self assembled to form nanofibers. Similar approaches have been used for other tissues such as cartilage, bone and cardiac applications, and show great promise in tissue engineering.

Microfabrication and nanofabrication approaches have also been used to modify surface properties with resolutions as small as 50 nm for controlling cell behavior. For example, topographical features that were a few microns across were used to orient cardiomyocytes and enhance their function (*32*). Studies have shown that nanopatterns can be used as means of orienting cells and guiding cell migration. Although much work needs to be done in understanding the biological mechanism associated with the effects of surface topography on cell behavior, the ability to engineer these properties has been useful for applications ranging from inducing the migration of an osteoblast on dental implants to controlling neurite outgrowth. In addition, microtopology and nanotopology can influence cell gene expression and migration and thus be incorporated into microfabricated tissue engineering scaffolds. For example, topographically patterned PLGA surfaces have been shown to induce alignment and elongation of smooth muscle cells (*33*) and to enhance the adhesion of several cell types such as endothelial cells and smooth muscle cells (*34, 35*).

Using micropatterning and nanopatterning, cell shape has also been shown to influence cell behavior. Changes in cell shape alter the cell cytoskeleton and influence cell fate decisions such as apoptosis, proliferation (*36*) and differentiation (*37*). Therefore, controlling cellular microenvironment using nanopatterning and micropatterning may be used for directing cell fate for tissue engineering applications. Therefore, it is envisioned that as the incorporation of such patterning approaches can be used to direct cell behavior to induce stem cell differentiation to generate desired cell types or be incorporated within 3D scaffolds to regulate cell behavior.

Conclusions

Nanotechnology is an emerging field that is potentially changing the way we treat diseases through drug delivery and tissue engineering. However, significant challenges remain in pushing this field into clinically viable therapies. For drug delivery, the design and testing of novel methods of controlling the interaction of nanomaterials with the body are some of the current barriers to translating these technologies to therapies. Methods of targeting nanomaterials to specific sites of the body while avoiding capture by organs, such as the liver and spleen, are major challenges that need to be addressed. With respect to tissue engineering, it is envisioned that new nanomaterials that provide proper signals and environmental cues to cells as well as generate 3D microenvironments may be advantageous over today's polymers. Nanoscale structures such as surface topography and patterning could be used to direct cell behavior. The incorporation of these strategies within tissue engineering scaffolds could further enhance their function. As Feynman had predicted, there has been plenty of room at the bottom to modify and enhance existing technologies by controlling material properties at nanoscale. Therefore, with sufficient time and research, the promise of nanotechnology based medicine may become a reality.

Ali Khademhosseini is a faculty member at Harvard-MIT's Division of Health Sciences and Technology and the Department of Medicine at Harvard Medical School and Brigham and Women's Hospital in Boston, Massachusetts. He has published numerous papers and has multiple issued or pending patents on the use of micro- and nanoscale technologies in biomedical applications. He has obtained many awards including outstanding undergraduate research mentor at MIT (2004), outstanding graduate student award by the Biomedical Engineering Society (2005) and outstanding research in polymer science by OMNOVA / MIT (2005). He obtained his Ph.D. in bioengineering from MIT, and MASc and BASc degrees from University of Toronto both in chemical engineering.

Robert S. Langer is one of 14 Institute Professors at MIT. He has written over 860 articles, and over 500 issued or pending patents worldwide. Langer has received over 130 major awards, including the Charles Stark Draper Prize, considered the equivalent of the Nobel Prize for engineers and the world's most prestigious engineering prize, from the National Academy of Engineering. He is the also the only engineer to receive the Gairdner Foundation International Award. Langer was elected to the Institute of Medicine of the National Academy of Sciences, National Academy of Engineering and the National Academy of Sciences. He is one of very few people ever elected to all three U.S. National Academies and the youngest in history (at age 43) to ever receive this distinction. He received his bachelors degree from Cornell University and his Sc.D. from MIT.