Convergence in biomedical technology

Ascher Shmulewitz, Robert Langer & John Patton

An entrepreneur and a pioneer in innovative technologies trade views with an industry veteran on the likely importance of convergent technology in health care.

Technology convergence is already a reality in communications, where it has generated new industry sectors. Increasing emphasis on translational research in biomedicine, together with the cross-fertilization of such fields as biotech, nanotech and information technology, now promise similar interdisciplinary, convergent solutions for disease prevention, screening, diagnosis, therapy, monitoring and management. Here, the views of an entrepreneur and a leading researcher on the potential of convergent biomedical technologies are contrasted with the historical perspective of an industry veteran.

The ascendance of combination products

Ascher Shmulewitz & Robert Langer

Despite the continued focus of governments and the pharmaceutical industry to develop drugs, many recent blockbuster products have not been traditional pharmaceuticals or biologics but technologies that combine drugs and medical devices[1]. For example, drug-device combinations have helped such companies as Johnson & Johnson (New Brunswick, NJ, USA) and Boston Scientific (Natick, MA, USA) to maintain a leadership position in the stent markets and have allowed Medtronic (Minneapolis, MN, USA) to dominate the pacemaker sector. Indeed, implantable pacemakers are becoming the primary therapy for many chronic diseases, including pain and central nervous system disorders.

The convergence of biotech, nanotech and information technology in new products will likely blur the distinction between the traditional turfs of the biotech, device and pharmaceutical industries (**Fig. 1**). Combination products result from the convergence of mature technologies. Senior executives of Johnson & Johnson and Medtronic have stated that, to achieve corporate goals, convergent technology solutions will be their major development focus and the next 'market revolution.' In the words of Ralph Larson, Chairman and CEO of Johnson & Johnson, "The future is combining devices and drugs"[2]. The market size of all convergent/combination products in 2004 was around $6 billion and is expected to grow to $10 billion by 2009 (ref. 3). It is estimated that nearly 90% of this market is related to cardiovascular medicine (of which 80% is drug-eluting stents); the rest comprises orthopedics and other surgical dressing products. In the United States, the majority of companies working on such combination products are located near San Francisco and Boston, close to the largest concentrations of venture capital resources. Although these companies are venture stage and are not yet generating revenue, nearly 70% are in the drug-device or drug-biomaterial cluster, whereas most of the others are related to information-communication technology.

Robert Langer is Institute Professor at the Massachusetts Institute of Technology in Cambridge, Massachusetts 02139, USA. e-mail: rlanger@mit.edu; Ascher Shmulewitz is at Medgenesis Partners Ltd in Tel-Aviv, Israel. e-mail: ascher@Incumed.com

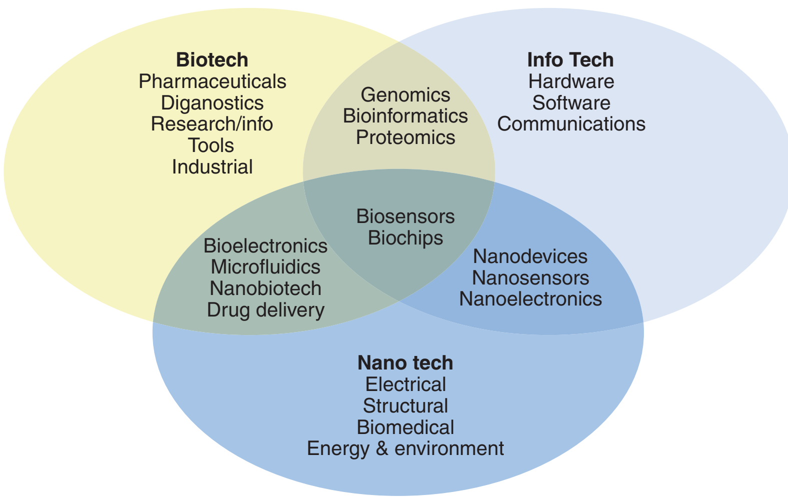

Figure 1 The convergence of two or more distinct scientific disciplines is the basis of a new device, process or product. When applied in the life sciences, the result is a new approach to prevention, screening, diagnosis, therapy, monitoring or disease management.

Convergent technologies also dovetail with the much-presaged, but yet to be realized transformation of medical practice from disease diagnosis and treatment to disease prediction and prevention. For example, smart implants may provide a means of remotely monitoring and managing therapeutic dosing; in turn, wireless communication with implants may allow health care services for chronic disease to shift from the hospital to the home setting.

Key drivers

The rise of convergent technologies is being driven by both scientific and economic trends. Scientific research is generating new, cross-disciplinary alliances. For example, the continuing miniaturization of integrated circuits has reached the molecular level, the traditional province of biotech and nanotech. The large research laboratories of computer companies, such as IBM (Armonk, NY, USA) and Hewlett Packard (Palo Alto, CA, USA) have developed substantial nanotech programs. Genencor (Palo Alto, CA, USA) is collaborating with Dow Chemicals (Midland, MI) to build a proprietary sillicon platform such as Ambri's (Chatwood, Australia) self-assembling lipid bilayer that incorporates gramacidin ion channels that act like biological switches, capable of detecting a range of substances *in silico* and directly generating electrical signals. Affymetrix (Santa Clara, CA, USA) is planning to manufacture biochips combine oligonucleotides and polarizable molecule monolayers that adhere to integrated circuits instead of transistors on computer chips. Indeed, Affymetrix has emerged as a clear leader in the oligonucleotide 'biochip' market, with 60% of a growing $400-million sector that includes application in mRNA expression profiling, single nucleotide polymorphism (SNP) resequencing and diagnostics. The combination of miniaturized microelectronics, novel biomaterials and adaptive signal processing techniques has created the possibility of building artificial neural implants—spurring new ventures, such as IMI (Intelligent Medical Implants, Zug, Switzerland), Optobionics (Naperville, IL, USA) and Cyberkinetics (Foxborough, MA, USA). The development of similar—and novel drug-delivery systems—is being pioneered by Medtronic and Alza (Mountain View, CA, USA).

Convergence technology development is also being fueled by business alliances. Such alliances allow market leaders with proven technologies or established marketing channels to find new uses for their core competencies while sharing the financial risk of an unpredictable regulatory path or public acceptance. Sun Microsystems (Santa Clara, CA, USA) and IBM have teamed up with numerous life-science companies to help accelerate the development of genomics and protein research. Oracle (Redwood City, CA, USA) has launched a $185-million collaboration in bioscience projects with Hitachi (Tokyo) and Myriad Genetics (Salt Lake City, UT, USA). Other examples of similar alliances[4] include the following: Boston Scientific's collaborations with Angiotech (Vancouver, BC, Canada), Corautus Genetics (San Diego, CA, USA), Advanced Bionics (Sylmar, CA, USA) and Osiris Therapeutics (Falls Point, PA, USA); Guidant's alliances with Novartis (Basel, Switzerland), Biosensors International (Newport Beach, CA, USA), SyneCor (Portola Valley, CA, USA) and MediVas (San Diego, CA, USA); Johnson & Johnson's deals with SurModics (Eden Prairie, MN), Wyeth (Madison, NJ, USA), BioPharm (Marshall, MI, USA), Orquest (Mountain View, CA, USA), Theratechnologies (Montreal, QC, Canada) and Transform Pharmaceuticals (Lexington, MA, USA); and Medtronic's partnerships with Abbott (Deerfield, IL, USA), Transvascular (Palo Alto, CA, USA), Genzyme (Framingham, MA, USA), Endobionics (San Leandro, CA, USA), Wyeth and Yamanouchi Pharma (Tokyo, Japan).

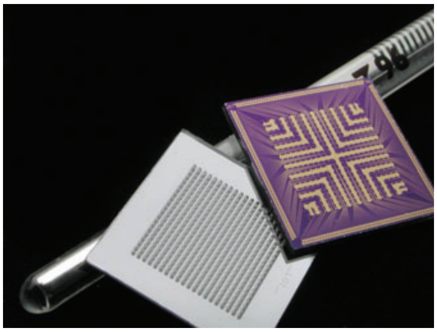

Figure 2 Place your chips. Will controlled release microchip, like this one, become an established means of drug delivery in the future?

Platforms to watch

The next ten years will witness the introduction of numerous convergent technology platforms that marry biology with medical devices and drug delivery systems. Areas with considerable potential for growth include tissue engineering, microelectrical mechanical systems, biomaterials, gene and protein delivery, targeted medicine, drug-device combinations and high-throughput technologies.

One of the most challenging of these areas is tissue engineering. It has been estimated that nearly half the cost of US health care can be attributed to tissue loss or organ failure[5]. The ability to create replacement livers, spinal cords, pancreases, hearts, kidneys and many other tissues and organs would radically decrease hospitalization time, relieve suffering and prolong life. Tissue engineering generally involves combining mammalian cells (including stem cells) with polymer materials in such a way as to create new tissues or organs. Although this area has been the focus for considerable research[6,7], many challenges remain. First, it will be essential to find cell sources that yield sufficient quantities of differentiated cells. Stem cells may represent an important source, provided that their differentiation, growth and immunogenicity can be controlled. Another possibility is autologous cells, although in many cases one may not be able to grow them quickly enough and in such a way that they maintain their differentiated state. A second challenge is ensuring that cells in engineered tissues survive. One promising approach is to develop methods for vascularizing three-dimensional cell masses using either microfabricated systems or the controlled release of growth factors[8]. A third major issue is immune rejection. Finding ways to prevent it—for example, through the use of somatic nuclear transfer—is clearly important but far from reduction to practice. Finally, there are practical issues, such as the shelf life of polymer-cell systems as well as scale-up and production issues. Despite these many challenges, the opportunities in tissue engineering are numerous[5].

A second major platform is microelectrical mechanical systems for use in sensing or drug delivery. An example is a controlled release microchip (**Fig. 2**). These systems are fabricated of silicon[9] or other materials[10] and contain wells that can be loaded with drugs and covered with caps made of gold or other substances. In the case of gold, applying a one-volt electrical signal to one or more of the wells dissolves the gold covers and releases the drug[9]. Challenges in this area include the development of appropriate drug formulations, of remote-control methods to regulate delivery by radiofrequency or telemetry and of miniaturized chips bearing their own power sources, microprocessors and even sensing systems. Because such chips can have hundreds or possibly thousands of wells containing either the same drug or multiple drugs at the same or different dosages (a 'pharmacy on a chip'), they may be well suited for delivery of new kinds of drugs, such as cancer chemotherapy drugs, in complex regimens[11]. They may also be useful for localized drug delivery; for example, they could be coupled with stents to treat restenosis. Finally, the wells could be replaced with sensors, creating new types of biosensing devices (e.g., for glucose).

A third area of interest is the development of new kinds of biomaterials for medical devices. Currently, most biomaterials are off-the-shelf materials that were originally used in consumer applications[12]. For example, polyetherurethane, the material used to construct artificial hearts, was first used in women's' girdles. Similarly, such materials as polyurethanes that are now used in breast implants were originally exploited for foam mattresses. Large-diameter vascular grafts are made of Dacron because it can be sewn easily and dialysis tubing is made of cellulose acetate, originally used in sausage casing. Significant opportunities exist for more rational design of biomaterials. One such approach is shape-memory materials, which are inserted through small holes during endoscopic surgery and then converted into a more bulky medical device by a temperature change[13] or by a fiber-optic lighting system[14]. For example, a surgeon could place a string-like object through a small endoscopic hole; a stimulus (e.g., temperature or light) would then convert it into an appropriately shaped medical device, such as a stent or a sheet. Shape-memory materials might also form the basis of self-tying sutures for use in minimally invasive surgery[13]. There are many other opportunities to design new biomaterials; examples include materials with improved biocompatibility, electrical conductivity, improved adhesion, bioactivity, piezoelectricity and novel surface chemistries.

A fourth area of application for combination technologies is the delivery of nucleic acid therapies. Viral vectors represent one approach; they are highly efficient and have tropisms for specific tissues but they also can cause serious safety problems. Alternatively synthetic vectors, such as liposomes or polymers, are potentially safer, cheaper and easier to manufacture but are currently far less efficient. A major challenge to successful gene therapy or synthetic small interfering RNA or microRNA therapy is the development of appropriate delivery systems, which is spurring efforts to develop novel polymers[15–17].

Another important area is the targeting of drugs to specific cells, such as tumor cells. This has been extremely difficult to accomplish for several reasons. One challenge has been to design micro- or nanoparticles that can travel throughout the blood stream without being taken up by untargeted cells, such as macrophages in the reticulo-endothelial system[18]. Another challenge is to design appropriate targeting moieties (e.g., antibodies, antibody fragments or aptamers[19]).

Beyond the agent itself used in targeting a drug to a tissue of interest, convergence technology may also expand the routes of administration available for the delivery of macromolecular drugs. Complex biologics, such as peptides or proteins, are generally given by injection, which must be aseptic, is often associated with scarring, may require qualified medical personnel for administration and poses disposal problems. New engineering principles, micromachining and nanotechnologies provide novel approaches for nasal, oral or transdermal delivery that may be more facile, effective or cheap than traditional needle-mediated delivery[20]. For example, in January Pfizer's (New York, NY) Exubera, an inhalable version of insulin, was approved by the US Food and Drug Administration (FDA) as an alternative to the injectable route. Elsewhere, drug-device combinations have already created clinical and market opportunities. For example, today, just over two years after FDA approval, polymer-based drug-coated stents—which combine drugs and materials with existing medical devices—represent a multi-billion dollar market. Many other drug-device combinations are possible, such as antibacterial/antifungal devices and new types of medicated devices to aid in surgery or to treat specific diseases.

Contrary to early claims that targeted medicine would reduce development times and costs, regulatory requirements will drive them up even further.

A last platform for convergent technology is the area of high-throughput biology and microarray technology. Industrial-scale approaches that enable experiments and data collection orders of magnitudes more rapid than in the past promise not only to transform basic research but also to ultimately lead to the development of new drugs and diagnostics. High-throughput technologies have already been used to discover new pharmaceutical formulations, such as new crystal forms of drugs, which has greatly accelerated pharmaceutical dosage form development[21]. They have also been applied to examine how materials control cell behavior, such as stem cell differentiation. For example, one of us (R.L.) has tested up to 70,000 material-cell interactions per day on an array of microdots, each containing a different material[22]. Similarly, peptide and oligonucleotide arrays[23,24] produced with photolithographic techniques promise to accelerate the identification of key biomarkers and the elucidation of groups of actors in biological pathways.

Of course, protein/peptide arrays present unique challenges[25]. Whereas nucleic acids share a common physical chemistry that is independent of sequence, proteins are very diverse in terms of hydrophobicity, charge and other characteristics. Therefore, protein structure and function may not be retained during high-throughput printing of protein arrays. Microarray fabrication techniques are another hurdle. Successful fabrication methods should be applicable to very different types of protein libraries and proteins must be attached to the array surface strongly and without denaturation.

Challenges going forward

Although they have numerous advantages, convergent technologies also have many perceived risks. Indeed, most industry experts recommend that combination products be avoided unless there are no alternatives. The convergence of genomics, diagnostics and therapies will lead inevitably to more personalized medicine, but many hurdles—scientific, regulatory, financial and social—must be overcome.

One major issue is higher development costs compared with conventional pharmaceutical products. The full development of a targeted medicine product will likely involve larger phase 2 studies and an additional perspective confirmatory phase 3 study for the identified patient subgroup. This product development cycle must be repeated to a large extent for each patient subgroup. Thus, contrary to early claims that targeted medicine would reduce development times and costs, regulatory requirements will drive them up even further. This belief has led the FDA to contemplate granting marketing exclusivity as an incentive to developing targeted medicine.

A second, related issue is a changing regulatory environment. Historically, the medical device and pharmaceutical sectors have operated under different sets of regulations in most developed countries. Regulators and lawmakers are reviewing existing regulatory pathways as a greater number of innovative combination products appear on the market and in the R&D pipeline. Biologic/device combination products offer unique challenges for any regulatory agency because of differing views of timelines, policies, development cycles and multiplicity of configurations. The normal review paradigm for biologics and devices is difficult to apply to combination products because of their interactions; therefore, development costs and times will most likely increase. At the FDA, the concept of 'primary mode of action' determines the jurisdiction of combination products. Historically, the FDA has interpreted primary mode of action based on the 'intended function' or 'purpose' of the combined product. A proposed reinterpretation, although not yet defined explicitly by the US Congress or FDA, seems to rely on the 'relative contribution of each component' of a combined product.

A third source of uncertainly is a complex product-development path. The integration of research-stage combination technologies into a product development program is always risky and tends to entail higher development and manufacturing costs. In addition, adding components from disciplines that are not part of the core business requires a more complex management structure and collaboration with unfamiliar business partners. This complexity, combined with the higher costs of regulatory compliance, slows the introduction and increases the entry costs of novel technologies.

A final concern is patient compliance. The drug-eluting stent, a metal scaffold used to treat occluded blood vessels, provides an instructive example. Up to 40% of patients who receive stents without an antiproliferative drug coating have an occlusion of the vessel within 6 months, whereas the long-term restenosis rates for drug-eluting stents from Johnson & Johnson and Boston Scientific are in the low single digits, leading to very rapid adoption of this technology. However, current drug-eluting stent treatments require long-term anti-platelet therapy—an off-label use for drug manufacturers. The result may be problems with patient compliance and an increased risk of heart attacks.

It should thus be emphasized that the adoption of convergent technologies and the benefits that accrue will be accompanied by the emergence of new risks. Healthcare providers have a responsibility to their patients to exercise caution in making the transition to this new paradigm. Convergence is about improving the ability of a provider to deliver a service or product; if rushed, it could undermine the ability to function and potentially increase costs.

Conclusions

At the broadest level, progress in convergent technologies will require new languages and institutional structures that cut across traditional disciplinary boundaries. Convergence products are still marginal in the life sciences, as demonstrated by the small number of publications (in 2005, we identified 30 on 'convergence,' 7,221 on 'combination products,' but close to 1 million in the medical device, biotech and pharmaceutical sectors).

Another goal should be to establish new interdisciplinary institutions relevant to the biotech/device interface. Graduates from these institutions will need to be trained in more than one scientific discipline and share a common technical language. What's more, a pool of skilled operators and practitioners will be needed to take advantage of the new technologies arising from the biotech/device industry. One need only look at the small number (around 300) of neuro-interventional practitioners in the United States to realize how this limits the therapeutic outcomes for the 750,000 individuals who suffer strokes each year[25].

Our ability to address the challenges posed by convergent technologies will depend on the pace of progress in biology, material sciences, chemical engineering and bioengineering. This is an interdisciplinary field that requires universities and research institutions to invest in cross-training programs that alert individuals to the opportunities and inspire them to enter the field. Given the transformation in medical practice promised by convergent technology, and the opportunities for economic growth, now is the time for a major research effort in the field. We believe it would be well worth the investment.

1. *Business Week* (May 3, 2005).
2. Frontline Strategic Consulting. *Combination Products: An Impact Analysis on the Convergence of Medical Devices and Therapeutics* (Navigant Consulting/ Front Line Strategic Market Reports, San Mateo, CA, 2003).
3. Soloninka, J. *Convergent Medical Technologies Local Impacts, Global Opportunities.* YORKBiotech Inaugural Meeting, Ontario, Canada, November 2-3, 2005.
4. Dubin, C. *Drug Delivery Today*, 4, (2004). published online May 2004 <http://www.drugdeliverytech.com/cgi-bin/articles.cgi?idArticle=235>
5. Langer, R. & Vacanti, J.P. *Science* **260**, 920–926 (1993).
6. Vacanti, J.P. & Langer, R. *Lancet* **354** Suppl 1, SI32–34 (1999).
7. Langer, R. & Vacanti, R. *Sci. Am.* **280**, 86–89 (1999).
8. Richardson, T.P., Peters, M.C., Ennett, A.B. & Mooney, D.J. Polymeric system for dual growth factor delivery. *Nat. Biotechnol.* **19**, 1029–1034 (2001).
9. Santini, J., Cima, M. & Langer, R. *Nature* **397**, 335–338 (1999).
10. Grayson, A. *et al.* Multi-pulse drug delivery from a resorbable polymeric microchip device. *Nat. Mater.* **2**, 767–772 (2003).
11. Moses, M., Brem, H. & Langer, R. *Sci. Med.* **9**, 264–273 (2003).
12. Peppas, N. & Langer, R. *Science* **263**, 1715–1720 (1994).
13. Lendlein, A. & Langer, R. *Science* **296**, 1673–1676 (2002).
14. Lendlein, A., Jiang, H., Junger, O. & Langer, R. *Nature* **434**, 879–882 (2005).
15. Luo, D. & Saltzman, M. *Nat. Biotechnol.* **18**, 33–37 (2000).
16. Hwang, S., Bellocq, M. & Davis, M. *Bioconjug. Chem.* **12**, 280–290 (2001).
17. Affleck, D.G., Yu, L., Bull, D., Bailey, S. & Kim, S.W. *Gene Ther.* **8**, 349–353, (2001).
18. Gref, R. *et al. Science* **263**, 1600–1603 (1994).
19. Farokhzad, O. *et al. Cancer Res.* **64**, 7668–7672 (2004).
20. Langer, R. *Sci. Am.* **288**, 50–57 (2003).
21. Gardner, C., Walsh, C. & Almarsson, O. *Nat. Rev. Drug Discov.* **3**, 926–934 (2004).
22. Anderson, D.G., Levenberg, S. & Langer, R. *Nat. Biotechnol.* **22**, 863–866 (2004).
23. McGall, G. *et al. Proc. Natl. Acad. Sci. USA* **93**, 13555–13560 (1996).
24. Schena, M., Shalon, D., Davis, R.W. & Brown, P.O. *Science* **270**, 467–470 (1995).
25. Langer, R. & Tirrell, D. *Nature* **428**, 487–492 (2004).
26. Levy, E.I. *et al. J. Invasive Cardiol.* **14**, 646–651 (2002)

A historical perspective on convergence technology

John S Patton

The convergence of technologies in the life sciences and medicine is not new. All innovative therapeutic devices, drugs or combinations have resulted from the convergence of technologies.

Nobody can take anything away from the true innovators and the marvelous new methods they are developing for the dissection and analyses of living systems. Equally awe-inspiring is the progress that is being made on the elemental design and fabrication of new therapeutic devices and drugs.

But the extraordinary complexity and redundancy of biology is often underestimated by even the most talented boosters and always oversimplified by the spread of buzzwords that give the public, investors and the media a distorted, overly optimistic view of the future which lacks, among other things, a clear sense of the relevant complexities that have been unearthed in the past. Developing convergent technologies requires tapping the minds and work of thinkers who can tap the past and do not attempt to oversimplify the future.

In 1986, I remember asking the head of research at Genentech (S. San Francisco, CA, USA) how we were going to deliver the new cloned neuroproteins into the brain. His answer: "Oh, we will just engineer around the blood-brain barrier."

We will, indeed—someday. To this day, however, engineering around the blood-brain barrier remains a formidable obstacle. To be sure, the biotech industry has made enormous strides. But sometimes experts in

John S. Patton is at Nektar Therapeutics and former head of drug delivery at Genentech. e-mail: jruddock@ca.nektar.com

this field think that just because they have figured out how to clear one barrier, they can clear the next one faster, cheaper, better. Cloning a protein is child's play compared with getting a large protein into the brain without drilling a hole in the skull.

Easier said than done

The development of inhaled insulin is a classic example of a development whose complexity was misunderstood and ultimately required far more time and money than even the realists originally predicted. This technology is the product of many different technologies and industries, and required the multidisciplinary talents of a vast array of experts. Fortunately, in January, their hard work paid off because the US Food and Drug Administration approved the world's first inhaled insulin.

Few outside of the narrow research and development field that produced this product can appreciate the biological and engineering complexity that this R&D feat required. But many will in the coming years, and they will invariably oversimplify it. And many will fail to learn from the lessons learned from this product-development quest—and from whence these lessons came.

The inhalation particles are made by spray drying, which is a typical food industry process. In this case, however, the technology is adapted for inhalable insulin by the development of new nozzles and cyclones that enable the formation and collection of 1- to 3-µm particles (in contrast to the food industry where 50- to 400-µm particles are made).

One of the lead engineers in the development of the insulin spray drying came from Caterpillar (Peoria, IL, USA), where he specialized in diesel carburetor design. The engineers that developed the novel fine-particle filling for the packaging of inhaled insulin dosages used technologies from the vibration and vacuum industries. And some of the engineers who developed the device for inhaled insulin came from scuba equipment design and the computer and printer maker Hewlett Packard (Palo Alto, CA, USA).

The idea for the extraordinary room temperature stabilization of the inhaled insulin formulation came from a keen understanding of the strategy employed by desert plants and invertebrates for maintaining protein stabilization during long droughts. And the appreciation of the unusual permeability of the lungs to insulin came from a marine biologist who studied intestinal fat absorption in fish.

Building truly convergent technologies represents multifactorial complexity in no small part because it requires the coordination of a multidisciplinary team of experts, each of whom has a very different notion about how to build things and why things work. Finding and managing this disparate pool of talent is one of the most overlooked and misunderstood challenges of developing convergent technologies. It is rare to find the compatibility required.

Compatibility conundrum

Compatibility is a key challenge that crops up time and again in the development of convergent technologies. A perennial challenge, for example, with most implantable devices is tissue compatibility. All objects implanted into the body are treated more or less as foreign. The most dramatic tissue reaction is formation of a capsule of tough connective tissue around the object, which can alter the movement of molecules in and out of the device and can make removal of the device difficult. An ideal device is one without significant tissue reaction, which is not felt and which does not require removal.

If there is one thing we should have learned by now about medicine, it is that human biology does not quickly, predictably or inexpensively yield its secrets.

There is much talk about the development of convergent technologies that will be implantable tissues and organs—some of them even produced from the patient's own cells. Although organ and tissue transplants have been used for some years now, the immune reactions against these foreign 'devices' have to be continuously controlled by immunosuppressive drugs that have numerous side effects. In order for new implanted living tissue to work seamlessly with the body, the body's immune system must think that the new tissue (device) is its own (that is, immune tolerance must be induced). The artificial pancreas has been on the verge of reality for many decades now.

Using stem cells as building blocks for more compatible tissue and perhaps even organ implant is being heralded as the next logical step. Rarely is it stated, however, that the challenges of putting something into a human body and then expecting this add-on to function within the body as if it was original equipment are daunting. We often fail to grasp that even if, or when, we reach the day that we can make an exact replica of a tissue or organ, we might not want it to interact with the body the way the original equipment did.

For example, even if one could simply reconstruct exact replicas of a type 1 diabetic patient's long lost insulin-producing beta cells, there is the risk that whatever immune reaction killed their original cells will still be there to kill the newly implanted ones once again. Time and research will solve these problems, but it will be longer and more expensive than we want. All too often we fail to sufficiently appreciate the awesome intricacies and mechanics of the human body.

Biology is kilogram, gram, milligram, micro, nano, pico and angstro. Most of the interesting features of the cell are nanometer in size or smaller and have been under intense study for years. The microchip, for all the nice nanosized features it contains, has little application for controlled release drug delivery—at least, as they exist for the foreseeable future—because most drug doses are in the tens or hundred of milligram range; they are far too massive to fit into the tiny spaces in a microchip.

The big problem with the next big thing

Waves of promising new technologies come and go and entrepreneurs and media never seem to grow tired of oversimplification and buzzwords. In the past, venture capitalists have swarmed and poured money into antisense, gene delivery, wound healing, rational design, genomics, proteomics, RNAi and now nanotech. If there is one thing we should have learned by now about medicine, it is that human biology does not quickly, predictably or inexpensively yield its secrets.

Real advances in medicine will continue to come from groups intensely focusing on a specific disease or drug delivery process, and bringing to bear on that challenge, every dang piece of ingenuity they can find—be it nano, micro or whatever. I can live with the idea and the words 'convergent technologies' so long as the objectives of the products that come from it are not oversimplified or wrapped in more buzzwords.